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Endocrinology

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Internal Secretions

May, 1921

ADRENAL INSUFFICIENCY

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I. PHYSIOLOGICAL DATA

When both adrenals are removed from most of the ordinary laboratory animals, e. g., dog, cat or guinea pig, death speedily ensues. The fatal result is not evaded, although it may be somewhat delayed, if the operation is performed in two stages and a considerable interval allowed to elapse between the removal of the two glands. The literature is enormous and is extensively cited in the monographs of Biedl (1) and Swale Vincent (2). We shall only refer to a few of the papers, especially as in the more modern work there is a general agreement in the results which particularly concern us.

Abelous and Langlois (3) found that hibernating frogs might live as long as 12 or 13 days after complete ablation of the adrenals, whereas summer frogs on the average never survived more than 48 hours. If the temperature of the room was kept about 22° C. the period of survival of winter frogs was much diminished. If a substantial fraction of one adrenal is left the animals remain entirely normal. If the portion left is very small, death ensues, but not so rapidly as after total adrenalectomy.

Albanese (4) confirmed these results, and from observations on the resistance to fatigue of the decapsulated frogs, concluded that a function of the adrenals is to destroy or transform toxic substances, especially those generated in muscular contraction, a suggestion also made by Abelous and Langlois (5). In another communication Abelous and Langlois (6) found that adult guinea pigs never lived more than 9 hours, and often only 5 hours after double adrenalectomy. Brown-

Séquard (7) in 1856 saw in guinea pigs a minimum period of survival of 9 hours and a maximum of 23 hours. The animals become rapidly weaker, paresis or complete paralysis of the hind legs may be seen and sometimes before death, convulsions. Removal of one adrenal has practically no effect.

Of rats, about 50 cent survive double adrenalectomy. Boinet (8) removed both adrenals in 75 grey rats and found that half of them survived. Many were in excellent condition 5 or 6 months later. The results were quite as good when the two glands were removed simultaneously as when the operation was done in two stages. Similar results were obtained by Stewart and Rogoff (9) in albino rats, although they did not keep them so long. It is astonishing, but characteristic of much of the work on this subject, that in rather recent papers Schwarz (10), Kahn and Starkenstein (11) it should be stated that rats do not survive more than a day when both adrenals are removed at one sitting. It is, of course, important to discriminate between the mortality due to the operation and that due to adrenal deficiency, and this is by no means easy when the animals die within a day or two. The size, age and nutritive condition of the rats are probably not without influence upon the result of removal of the adrenals, certainly as regards the surgical risks in those small animals, and perhaps also as regards the consequences of adrenal insufficiency.

The great majority of rabbits die after double adrenalectomy, but some survive even where the glands are excised at one operation. When the operation is done in two stages, about one in five of the animals survive under good conditions, and after some weeks these rabbits are not distinguished from normal animals by any striking peculiarities. The result of Strehl and Weiss (14), that of 26 rabbits, all died in 8 to 14 hours after double adrenalectomy must have been due to faulty surgery. The rats operated on by them also died in 15 to 19 hours.

Elliott (15) found that 19 out of 21 cats in which both glands were excised at one and the same operation died in from 18 to 48 hours (generally on the second day). Only 2 cats survived to the 9th and 10th day respectively. Of 25 cats from which the glands were removed in two operations 9 died on the 2nd or 3rd day. Thirteen of the animals lived for 6 to 10 days; two survived to the 22nd and 23rd day, and one seemed to have recovered completely when it was killed in the 9th week. These details are quoted because in the question of the time of survival after removal of both adrenals the results of modern work, done with good surgical technique, are much more important than much of the older work, such as that of Strehl and Weiss (14), where some of the deaths attributed to adrenal insufficiency were undoubtedly due to shock (especially in the case of the smaller animals) and others to infection. Elliott attributes the longer periods of survival to compensatory hypertrophy of small accessory adrenals of cortical tissue.

All good observers agree that in practically all dogs double adrenalectomy is incompatible with life. Langlois (16) found that apart from complications connected with the operation all dogs survived removal of one adrenal. Removal of the second gland after an interval of 15 days to 5 months was invariably followed by rapid death (10 to 52 hours, average 28 hours). When both glands were removed at one time the average period of survival was only 17 hours, with a maximum of 26 hours. As is pointed out in the paper, it is impossible to say how much of this slight difference is due to the greater severity of the operation as such. Langlois suggests that observers, like Giliberti and Di Matei (17), Tizzoni (18), and others who saw some dogs sur-

vive for a long period must have left behind a portion of the adrenal tissue owing to faulty technique. The current explanation for the survival of so many rabbits and rats is that accessory adrenal (cortical) tissue is more frequently encountered and is more abundant in these than in the other laboratory animals. In a general way this may be true, but it must be said that in many cases of long survival, such accessory tissue is not discoverable, at least by careful macroscopic examination, nor when discoverable does its total mass often equal the fraction of the total mass of adrenal substance which must be left behind to prevent death in animals like the dog, cat and guinea pig.

A few of the animals which die after removal of both adrenals no doubt, even under the best conditions, in extensive series, succumb to accidental surgical consequences of the operation (shock and infection). With good technique this is a quite unimportant factor. Intercurrent diseases known to affect laboratory stock, sometimes account for a certain number of the deaths. But there can be no doubt that in the vast majority of cases the animals die from "adrenal insufficiency," from the loss, that is to say, of the indispensable something which the adrenals contribute to the functioning of the body. What are the symptoms associated with the extreme degree of adrenal insufficiency caused by the removal of both adrenals in animals? It is disappointing to say in view of the prominence assumed by "suprarenal insufficiency" in the speculations of many clinical observers, who cannot know till after the death of the patient, if then, whether there is any defect in the quantity or physiological quality of the adrenal cortex or medulla, that the symptoms observed by physiologists in animals in which they have purposely produced a known amount of adrenal deficiency, are by no means definite, sharp and characteristic. To be sure, the animal, which may have recovered well after the final operation, and may exhibit a normal temperature, and an appetite and power of muscular effort not sensibly different from that of a control animal subjected at the same time to a similar operation, not involving interference with the adrenals, may rather abruptly begin to show loss of appetite, muscular weakness and a temperature below the normal, and in 24 or 48 hours or less, may be dead. But there is nothing specially pathognomic in such symptoms unless indeed it be the muscular weakness, which may seem to come on with more rapidity than is usually seen in animals dying under other conditions. Elliott (15) says that "all the cats" which survived for the longer

periods "lost weight, and those which survived longest became extremely thin. This was partly due to a loss of appetite. The approach of death was always announced by a very characteristic weakness. The eyeballs lost their tension and became soft as the blood-pressure steadily fell. Special care had to be taken by artificial warmth to check the fall of body temperature, for otherwise the rectal temperature would have dropped from 103° or 104° F. to 85° or 90° F. ere death ensued." We have seen all these symptoms in cats dying after reduction of the total adrenal substance beyond the necessary minimum. But we have no confidence that if shown the animals, without knowing what had been done to them, we could make the diagnosis of adrenal insufficiency. There must, of course, be some profound disturbance of function but the essential manifestations of that disturbance have hitherto remained obscure.

It might be thought that if the process were rendered more chronic by removing only a portion of the adrenal substance, a more definite clinical picture of adrenal insufficiency would be revealed. In the case of the pancreas, it is known that in the dog, so long as a fifth, or even somewhat less, of the total mass is left, no permanent symptoms ensue (Minkowski and von Mering (19)). When one-ninth to one-eighth of the pancreas is left the symptoms come on more gradually and are more dependent upon the character and amount of the food than if the organ is totally extirpated or than if a still smaller fraction (1/10) is spared, and the resemblance of the condition to moderately severe diabetes in man becomes more close (Thiroloix (20), Allen (21)). In the case of the adrenal, however, it has not hitherto proved possible, or only in a very limited degree, to realize a similar gradation in the severity of the symptoms, when varying proportions of the total gland substance are taken away. Trim and pare as he may, the operator either leaves so much of the gland that the animal survives indefinitely in good health, or takes away so much that it dies quickly, as it would have done if the glands had been totally excised. The anatomical line which separates full physiological sufficiency from fatal insufficiency is so narrow that a certain small fraction of this peculiar loaf seems to be, in some cases, so much better than no bread, that it is apparently as good as

the whole, while, in other cases, it seems to be no better than a stone. It must be remembered, however, in comparing the adrenals with the pancreas that from the shape and dimensions of the two objects, it is probably easier in the case of the latter to purposely leave behind a given fraction of the gland substance than in the case of the adrenals. The damage due to interference with the blood supply, including that possibly due to thrombosis, cannot be precisely known, and must vary in each case. The amount of accessory adrenal tissue, hypertrophied in variable degree after the first operation, and the amount of hypertrophy in the portion of the adrenal left, if the animal lives some time, are also factors which cannot well be accurately controlled.

According to Langlois (16) when about 1/6 to 1/11 of the total mass of the adrenal tissue is left in dogs, survival is possible. Far too much emphasis has sometimes been placed on these figures, which, as the author points out, are not to be taken in an absolute sense. They are rough estimates of the amount of tissue unintentionally left behind in a very small number of the animals. Hoskins (22), and Whipple and Christman (23) have supplied better data on this point. The former found that dogs survive after removal of as much as 7/10 of the total mass of the glands, and the latter observers give examples of dogs in which 1/6 or perhaps even a smaller fraction of the adrenal tissue sufficed.

Biedl (1) speaks of one-eighth as the proportion which must be left in dogs, cats and rabbits. Abelous and Langlois (6) stated that the removal of one adrenal had little effect upon guinea pigs, although they might lose weight for a time. After considerable destruction of both glands by the cautery survival was still observed, and even when the amount of tissue destroyed was so great that indefinite survival was not possible the animals lived much longer than after complete adrenalectomy. Elliott mentions that he found it impossible to excise even one adrenal in the English guinea pig at one operation, without causing death, although one adrenal can be removed piecemeal. This, however, does not apply to the variety of guinea pig termed by dealers here the "English guinea pig," in which excision of one adrenal causes no symptoms, even when followed later by removal of a large portion of the other (Stewart and Rogoff). It is not definitely known whether age is a factor in the results of such operations, although susceptibility to shock may be greater in small than in large adult guinea pigs. Gates (24) found that it was possible to remove 3/4 to 7/8 of the adrenal tissue from guinea pigs without causing symptoms of adrenal insufficiency. We can confirm this. In a large series of guinea pigs it was found that even as little as 1/9 or 1/10 of the total mass sufficed. Even after total adrenalectomy (at two sittings) in 7 guinea pigs, 5 of the animals lived 5 to 9 days after removal of the second adrenal. One is still alive after 9 days and another after 14 days.

The results of Rogoff and myself on cats agree with those of previous workers. In the first operation, a varying fraction of one adrenal (usually the right) was removed. When the animal had sufficiently recovered from the effects of the operation, the whole, or, in a few cases, a portion of the remaining adrenal was excised. Of

18 animals, 2 died of distemper after removal of the greater portion of one adrenal, and the experiment could not be completed. Five cats have survived, all in good condition. In one of these the left adrenal and one-third of the right were excised at one operation. In another, 3/5 of the right adrenal was removed and, 18 days thereafter, the whole of the left adrenal. In another 1/3 to 2/5 of the left adrenal, and, 22 days thereafter, the whole of the right were excised. In the fourth cat nearly the whole of the right adrenal (at least nine-tenths, as was judged) was taken away, and 16 days thereafter 2/3 to 3/4 of the left gland. In the fifth cat 2/5 of the right and, 18 days thereafter, all of the left gland was removed. In the eleven cats which died, the interval between the two operations was about the same (16 to 27 days). They usually recovered well after the second operation, took food and showed no symptoms for a time. Then they refused to eat, showed signs of muscular weakness, often a subnormal temperature, became lethargic and died. Some notes are appended.

Cat 4. Male. Excised 3/4 to 7/8 of right adrenal and 24 days thereafter the whole of the left adrenal. Apparently normal for 6 days after last operation, then developed the symptoms mentioned and died 24 to 36 hours after.

Cat 5. Male. Excised 9/10 of right and 17 days thereafter the whole of the left adrenal. Good recovery. Animal seemed well for 5 days, when it was noticed that the hind legs appeared weak, and that food was not being taken. Died in 24 hours.

Cat 6. Male. Excised 7/8 of right, and 17 days thereafter all the left adrenal. Recovered well and was very active for 6 days, when it seemed to be weaker. It lived still more than 5 days, getting continuously weaker and taking very little milk. Rectal temperature the day before death was still 38.4° C., pulse 220, respiration 24.

Cat 7. Male. Excised 2/3 to 3/4 of right and 17 days thereafter the whole of left adrenal. Post-operative recovery somewhat slower than usual, but on second day after last operation it seemed fairly well. On the third day it became lethargic and apparently weak, especially in the hind legs. Temperature 36.2° C., pulse 208, respiration 32. It died 5 days from the last operation.

Cat 9. Female. Excised somewhat more than 3/4 of right, and 21 days thereaafter the whole of left adrenal. Recovery was good for about a day. Then the animal became progressively weaker. On the 5th day after the last operation the temperature was 35° C., pulse too feeble to count, respiration 40. It died the ensuing night.

Cat 10. Male. Excised 9/10 of left and 21 days thereafter all of the right adrenal. The animal became progressively weaker and died 3½ days after last operation. The day before death, the temperature was 35.3° C., respiration 36, pulse too weak to count.

Cat 13. Male. Excised 1/3 to 2/5 of left, and 22 days thereafter the whole of right adrenal. Recovery was excellent, and cat was in good condition till the eighth day, when weakness in the hind legs became apparent and food was taken sparingly. Two days later it died. Temperature on last day 35.1° C., pulse 180, respiration 42.

Cat 16. Male. Excised 2/3 to 3/4 of right, and 18 days thereafter the whole of left adrenal. The day after the last operation the temperature was 34.5° C., respiration 32, pulse too weak to count. The animal died during the night.

Cat 17. Female. Excised 7/8 to 9/10 of the right, and 16 days thereafter about 2/3 of the left adrenal. The animal began to show weakness the second day after the last operation, and died in the night between the 3rd and 4th day.

Cat 20. Male. Excised 9/10 of right adrenal. The animal developed distemper but recovered; 27 days after the first operation excised 2/3 to 3/4 of left adrenal. It was observed that the left adrenal was very large (hypertrophy after the first operation). The animal was in good condition for a day after the last operation, then gradually weakened and died between the third and fourth day. It was confirmed at autopsy, that the remnant of the left adrenal was decidedly larger than the minimum amount which must ordinarily be retained to prevent death. Two possibilities might be suggested. Either the demand on the adrenals was greater than ordinary in this cat, as indicated by the great hypertrophy of the left adrenal after the first operation, because of the paucity or absence of accessory adrenal tissue or for other reasons, or the tissue of the enlarged adrenal did not possess a physiological value in proportion to its bulk. In this connection it may be remarked that hypertrophy of the adrenal is often observed when far more adrenal tissue remains than is necessary for life and health. For instance, when one adrenal is removed the other hypertrophies. This is seen with the greatest constancy in rabbits, but is common in cats. Yet at the original operation a large fraction of the adrenal which is destined to undergo hypertrophy could have been removed without producing symtoms. Elliott (15) has made the interesting observation that in his experiments on total removal of the adrenals, the cats which survived excision of the second gland for the longer periods rarely showed any enlargement of the second adrenal, compensatory hypertrophy having occurred in small accessory adrenals. On the other hand, in the cats which died soon after removal of the second adrenal that gland was hypertrophied.

Hartman and Blatz (25) endeavored to reduce the adrenal function less drastically than by total removal of the glands, by tying the adrenal veins. They found that most of the animals (cats and dogs) lived much longer than after total adrenalectomy, although they eventually died. No specially characteristic symptoms were developed. Several of the animals showed "symptoms of weakness some time before death."

Up to the present, then, it has not been possible to produce experimentally any well characterized symptoms associated with partial adrenal insufficiency. That changes, and profound changes take place when the adrenal tissue is removed below a certain limit is not arguable, for life can no longer be maintained, and changes which render death inevitable are surely important. It is extremely probable that the essential changes are metabolic, but little real progress has been made in discovering definite quantitative or qualitative alterations in the metabolism, or in relating such alterations as have been assumed to occur to the fatal adrenal insufficiency. The too often quoted statement that the blood sugar content is diminished after total adrenalectomy in dogs (Bierry and Malloizel (26), Porges (27)) rests upon the frail foundation of observations on practically moribund animals. The rapidly increasing weakness and the fall of blood pressure in animals

hastening to die, are not sufficiently specific symptoms to make it very safe to link them up with the loss of adrenal function. In animals which survive with a vast anatomical deficiency in adrenal tissue it is very difficult to unveil any signs of corresponding physiological insufficiency. The temporary emaciation noticed by Abelous and Langlois (6) in guinea pigs after partial destruction of both glands or even after removal of one, is also not easy to interpret, (in animals recovering from a considerable operation,) as a sign of the loss of a specific adrenal function. The observations of Whipple and Christman (23) that the excretion of phenol-tetrachlorphthalein in the bile is diminished when three-fourths or more of the adrenal tissue has been extirpated in dogs, and is again increased if the remaining tissue hypertrophies, is suggestive. Pancreatic deficiency is associated with a similar drop in phthalein excretion, and it would be difficult to say whether the change is associated with a general deterioration of the animal or directly with the loss of some specific endocrine function.

Elliott (15) was unable to demonstrate any alteration in the mechanism of the heart beat during the gradual failure of the circulation in cats after total adrenalectomy until death. There was no paralysis of the skeletal muscles or their nerves, and no paralysis of the cardiac vagus fibres. But when the animals had become very weak and were moribund, there was some paralysis of the efferent vasomotor nerves, and only a slight rise of pressure was caused by nicotin. Hoskins (22) observed also in dogs which survived the removal of one-half to seven-tenths of the adrenal tissue that the vasomotor reaction to nicotin was decreased, and concluded that partial adrenal deficiency results in a depression of the excitability of the sympathetic nervous system proper; this depression being probably only one phase of a generalized interference with fundamental metabolism.

The view has been industriously developed by certain writers that the secret of the adrenal function lies in the reciprocal action of the gland and other endocrine organs, particularly the thyroid and the pancreas (Eppinger, Falta and Rudinger (29)). Gley and Quinquaud (30) very naturally express astonishment at the ease with which such theories

gained a considerable degree of acceptance without ever having been subjected to a direct experimental investigation. Lusk and Riche (31) have shown that not one of the statements as to the supposed rôle of epinephrin in metabolism and its action upon the endocrine organs (pancreas and thyroid), upon which the theory of Eppinger, Falta and Rudinger was based, is true, and that the theory is not tenable in any of its particulars. It has been demonstrated by Stewart and Rogoff (9) (32) (33) that contrary to the statements of a number of observers, the adrenals are not essentially concerned in the experimental hyperglycemias caused by piqûre, ether anesthesia and asphyxia, since these hyperglycemias can be well obtained in rabbits which have survived double adrenalectomy and in cats whose epinephrin output has been greatly diminished or abolished by removal of one adrenal and section of the nerves of the other.

Recently Hédon and Giraud (34) have come to the conclusion, that in dogs extirpation of the pancreas is not followed by hyperglycemia if the adrenals are removed either before, or immediately after the extirpation of the pancreas. If the adrenals are partially destroyed the usual hyperglycemia follows pancreatectomy. Contradictory results have been obtained by other observers. As it is the epinephrin given off from the adrenals which has always been considered the important thing in these theories, a much better experiment could be made upon dogs which had recovered completely after the operation for suppression of the epinephrin output (removal of one adrenal and section of the nerves of the other) than in dogs which have just been anesthetised for the performance of two severe operations.

The observation that feeding with thyroid substance is associated with hypertrophy of the adrenals, and a corresponding increase in their epinephrin store (Herring (35)) has not been confirmed by Kuriyama (36), who considers that the variations seen by Herring are not beyond the normal range. Hewitt (37), however, has pointed out that in certain respects Kuriyama's experiments differed from those of Herring. And other observers, (R. G. Hoskins (38) and especially E. R. Hoskins (39)) have also obtained adrenal hypertrophy after

feeding with thyroid. It is necessary to remark, however, that there is nothing specific about the increase in size of the adrenals, since similar hypertrophy is found in other organs, including the pancreas (E. R. Hoskins (38) Kojima (40)). Many infections and intoxications have been shown to be associated with enlargement of the adrenals (Langlois (41), Porak (42) et al.), although enlargement due to edema (and congestion) has not always been discriminated from true hypertrophy. Mulon and Porak (43) found that in animals employed for the production of antibodies of various kinds the adrenal cortex was hypertrophied. Porak (42) says that the largest adrenals seen by him were in rabbits repeatedly injected with sheep's erythrocytes for the production of anti-sheep serum for the Wasserman test in the municipal laboratory at Paris. He remarks apropos of the innumerable researches on the condition of the adrenals in infections and intoxications before his own work, that the existence of the same histological changes in the adrenals in infection and in immunity prove in a definite fashion the excesses of the theory of adrenal insufficiency in infections and intoxications. It is as welcome as it is unfortunately rare at the moment, to find in the French clinical and pathological literature a protest against the fetish of adrenal insufficiency. Gley and his co-workers have given but a cool reception to the complementary doctrine of what may be almost termed "adrenal all-sufficiency" in physiology.

The risk of deducing a special physiological relationship between the thyroid and the adrenals merely because the adrenal hypertrophies under the influence of thyroid feeding, is further illustrated by the fact that removal of the thyroid may be similarly associated with adrenal hypertrophy (Gley (44), Carlson (45), Stewart and Rogoff (46)). The adrenals seem, indeed, to vary much in size, like the thyroid, and under many physiological and pathological conditions. Thus, Guiyesse (47), Watrin (48), Verdozzi (49) and other observers consider their hypertrophy in pregnancy as a normal physiological event. Verdozzi finds a still greater effect during lactation. Mahnert (94) has based on the more than dubious Abderhalden reaction the contention that in pregnancy a de-

rangement of function (dysfunctioning) of the adrenals occurs. This appeal to the Abderhalden reaction recalls Gibbon's famous footnote: "Abu Rafe was an eye-witness, but who will be witness for Abu Rafe?" Hatai (50) has asserted that the adrenals hypertrophy in female rats subjected to prolonged muscular exercise daily for several months. C. A. Stewart (51) observed a progressive increase in the size of the adrenals in young rats underfed for long periods. Jackson (52) has also observed changes in the adrenal in rats during inanition. Byrne (53) states that in 8 soldiers dead from underfeeding in a German prison camp the suprarenals were enlarged to almost 1½ times the normal size. Microscopically the enlargement seemed to be mostly in the cortex. McCarrison (54) has also described enlargement of the adrenals in inanition and on a scorbutic diet, and Vincent and Hollenberg (55) have confirmed his findings. Some observers have noted a reduction in the lipoids of the cortex in inanition. But Elliott (57) states that the lipoids were not reduced in cases of disease associated with practical starvation (anorexia, cancer of the stomach). Grabfield and Squier (56), have recently announced that under the influence of Roentgen rays applied to the locality of the adrenals in the rabbit, hypertrophy occurred.

The question whether experimental adrenal insufficiency is due to the loss of the cortex or of the medulla, or of both has been much discussed. The experimental evidence has tended more and more to show that the cortex is the part of the adrenal indispensable for life. It is the cortical tissue which alone, or at any rate most conspicuously undergoes compensatory hyperplasia, when a deficiency is created by removal of a considerable part of the adrenal tissue. The accessory adrenal tissue, which also undergoes hypertrophy under these circumstances, and which is usually supposed to be responsible for the survival of those animals which do not succumb to loss of both adrenals, consists entirely of cortex. Only the cortical tissue can be successfully grafted. When one adrenal is completely removed and only a small portion (⅓ to ⅕) at one pole of the other adrenal left, it is probable that in many instances the viable portion of the remnant consists entirely of

cortex. Wheeler and Vincent (58) have destroyed practically all of the medulla in dogs without causing death.

In cats, dogs and macaque monkeys it has been seen that great diminution or suppression of the epinephrin output of the adrenals after removal of one gland and section of the nerves of the other, is compatible with indefinite survival of the animal in good health, (Stewart and Rogoff (59)). It is little more than a trick of special pleading to urge that the extra-capsular chromaphil tissue may be sufficient to supply the indispensable epinephrin output. If there is any epinephrin given off from the scattered chromaphil tissue the output must be of a different order of magnitude from that of the adrenal medulla. Kahn (60) has attempted to show that in the dog the abdominal chromaphil body (paraganglion) does give off epinephrin. But the experiment is very difficult to carry out without fault. He used Trendelenburg's method (61) of perfusion of the hind legs of frogs (Läwen preparation (62)), and it is well known that serum contains a vasoconstrictor substance other than epinephrin which makes it difficult to accurately assay the epinephrin content of serum on such an object. Most of Kahn's curves do not show any very great difference between serum from the cava blood and serum from the abdominal chromaphil body. But Kahn himself states that even in the dog, where it is relatively greater in amount than in most other animals, the whole mass of the extracapsular chromaphil tissue is insignificant, compared with the suprarenal medulla. It must be pointed out also that if there is any physiological liberation of epinephrin from the diffuse chromaphil tissue it is highly probable, judging from the analogy of the adrenal medulla, that this liberation is under the control of nerves. If so, in cases where the splanchnics have been cut, or the dorsal cord divided, it would seem practically certain that the innervation of the greater portion of the extracapsular chromaphil tissue must have been interfered with. Yet such operations, even when added to the operation practiced by us for the suppression of the adrenal output, do not cause death, as removal of both adrenals does.

Vincent (63) points out that from the relatively large size of the abdominal chromaphil body in the dog, this animal

might be expected to be more resistant to extirpation of the adrenals than other animals, if the chromaphil tissue were essential. But the dog does not survive the operation, whereas the white rat, in which Vincent failed to find any traces of "extra-suprarenal chromaphil tissue," is the most resistant of all laboratory animals. In the monkey, also, no extracapsular chromaphil tissue has been recognized with certainty. Yet the monkey is not affected by interference with the epinephrin output of the adrenals.

It is a curious thing that while the great bulk of the experimental evidence emphasizes the importance of the cortex without demonstrating any definite physiological value for the medulla, or at least for its epinephrin secretion, the bulk of clinical writers seem almost to ignore the existence of the cortex. "Adrenal insufficiency" in nine clinical papers out of ten, so far as they have come to the notice of the present writer, seems to connote interference with the output of epinephrin and consequent derangement of functions in which epinephrin is assumed to play a leading rôle. Worse still is the confusion between the rate of epinephrin output and the magnitude of the epinephrin store. It is very common indeed to find the conclusion drawn that because the epinephrin store was found smaller than the average, perhaps, many hours after death, the "adrenal function" must have been depressed and the patient must have suffered from adrenal insufficiency during life. It would be just as correct to conclude that if the liver of an animal, kept at rest in a warm room and fed with a definite food ration, contained 5 per cent of glycogen, while the liver of another animal, fed in the same way but allowed, or compelled to move around freely in a cool room contained but 1 per cent, the "hepatic function" of the latter was depressed and it was suffering from hepatic insufficiency. It ought to be recognized once and for all that the stock of epinephrin present at any moment in the adrenal medulla is simply a balance, related no doubt to the relative rates of formation and of liberation of epinephrin, but giving no clue to the rate at which the epinephrin is being given off. A striking illustration of this is the fact discovered by Elliott (64) that after section of the nerves going to one adrenal the store after a day or two is found to be the same

in the innervated and in the denervated gland. Yet the latter, if section of the nerves has been thorough, is giving off no detectable amount of epinephrin, not even one-hundredth or one-thousandth of the amount being liberated by its fellow (Stewart and Rogoff, 59). To those who estimate the activity of "adrenal function" by the magnitude of the epinephrin store, the two glands would be equally active. Yet this they cannot be if their function is concerned with anything which epinephrin liberated from the adrenals can do in the body.

There is no evidence that diminution in the ordinary rate of epinephrin output or even its total suppression can give rise to symptoms, even in such physiological emergencies as have been supposed to increase the demand for epinephrin. For instance, it has not proved possible to demonstrate any incapacity in animals, deprived of epinephrin from the adrenals, to support the fatigue of enforced muscular effort, as compared with normal animals. Although deficiency of cortical substance, carried to a certain point, produces decisive changes leading more or less speedily to death, the essential changes do not lie on the surface, and no definite, clean-cut symptoms characterize the clinical picture of an animal dying from experimentally produced adrenal insufficiency. In the case of the cortex also, when the amount of adrenal substance has been greatly reduced, but not so much as to cause death, the repeated subjection of the animal to such a physiological emergency as severe muscular exertion, does not reveal any difference between these animals and animals with intact adrenals. It is widely believed that muscular weakness is a symptom of adrenal insufficiency, and often assumed that it is deficiency of the epinephrin output which is the important thing. If either the medulla or the cortex is closely related to the proper functioning of the neuro-muscular machine, or exerts any appreciable influence upon the processes underlying muscular fatigue (Gruber, 13), it might be thought likely that repeated spells of severe muscular exertion, in an animal on the borderline of actual anatomical deficiency of adrenal tissue, would suffice to develop a physiological deficiency, where none would have developed in an animal at rest. In our cats, however, no difference was revealed between the normal animal and the

animal with perhaps only 1/6 or 1/8 of its adrenal mass. Boinet (65) also found that rats which had survived double adrenalectomy for 5 or 6 months, withstood extreme muscular exertion quite well. Considering the small number of normal controls employed, and the great variability in the length of time necessary to produce absolute fatigue, it cannot be said that he made out any difference between the decapsulated and the normal rats. We have found a definite deficiency in the epinephrin store of the still innervated adrenal, as compared with its previously denervated fellow, in cats after muscular exertion carried to the point of great fatigue.

On the whole, then, it must be granted that hitherto the attempts made to evoke in animals a well marked syndrome characteristic of adrenal deficiency, have been singularly disappointing. The contrast is great when we leave this desert, where the physiologists and experimental pathologists have wandered, striking many rocks but finding few springs, and pass into the exuberant land of clinical endocrinology, flowing with blandest milk and honey almost suspiciously sweet.

II. SOME CLINICAL VIEWS

It is impossible to mention more than a few of the conditions discussed in innumerable papers, in which adrenal insufficiency has been assumed to play a part. A rank growth of "endocrinological" speculations sprang up during the war, which developed so many novel medical problems, all of course pressing for solution, few of which could be quickly solved. But hypotheses could be quickly framed, especially when the framers were not hampered by any excess of critical faculty or exact physiological knowledge. The most recent "ology," endocrinology, was naturally pressed into the service. Much of this speculation unfortunately found its way into print, in spite of the scarcity of paper, and scarce paper was sometimes ill applied in this service.

Even in the case of Addison's disease, the majority of clinical writers seem still to suppose that it is the loss of the epinephrin secretion of the medulla which is the important thing, although experimental physiology affords no basis for such a view. That the epinephrin store of suprarenal glands

extensively destroyed by tubercular disease, should be deficient or reduced to vanishing point is inevitable, but this fact throws no light upon the production of the syndrome.

Claude and Gougerot (66) put forward in 1908 what they considered as a new conception, that certain complex symptoms are due to primary insufficiency of more than one of the endocrine glands. There is no reason in the world why this should not be true. But the evidence adduced from the clinical study, followed by autopsy, of one case, is singularly unconvincing. We are only concerned here with insufficiency of the adrenals. But they state that insufficiency of the thyroid, of the testicles and of the suprarenals was diagnosed during life and verified at at autopsy. The patient was tubercular, and there was asthenia. A diffuse pigmentation appeared not long before the patient's death, on certain parts of the face. The blood pressure fell to 100 and even to 90 mm. of mercury. The adrenals were found to weigh only 5 grams, less than half the normal weight. Histologically both cortex and medulla were fairly normal, apart from the smaller volume, especially of the medulla. There is certainly nothing here which, so far can be judged from the results of experiments on animals, lends any support to the idea that adrenal insufficiency was the cause of any of the symptoms. In man a very small portion of the suprarenal tissue has sometimes been found intact at autopsy, although the person almost up to the time of death may have been apparently normal and capable of hard physical work. Boyd (67) for instance, describes the case of a soldier who died while on leave of absence. He was apparently well just before he was found semi-conscious in his room. He had been performing his duty in a training camp and showed no signs of Addison's disease. The autopsy showed that the lungs were to some extent affected with tuberculosis. The adrenals were almost entirely converted into "'structureless" masses larger than the original glands. On the right side neither cortex nor medulla could be found. On the left side a narrow strip of cortex not more than 2 mm. in width was present at one point, but no medullary tissue. Although the author attributes death to acute adrenal insufficiency, this is, of course, hypothetical, as no signs of adrenal insufficiency (if there are any definite signs) were observed dur-

ing life. The only safe conclusion, which the author does not fail to draw, is that the medulla is not essential to life. This case seems further to illustrate the fact, established by experiments on animals, that the preservation of only a small portion of the cortex may be compatible with apparent health and vigor.

Brock and Kay (68), discussing a clinical syndrome somewhat allied to that described by Claude and Gougerot, come to the conservative conclusion that "Since we regard the white line of Sergent as being a very doubtful sign of hypoadrenia, and with no other certain evidence of deficient suprarenal secretion, the participation of this gland seems very doubtful." Sergent (69), like many other clinical writers, seems to consider hypoadrenia as synonymous with adrenal insufficiency. If by hypoadrenia he means diminished output of epinephrin, there is not one experimental fact which shows that this would produce any symptoms at all. "Arterial hypotension" is not caused even when the epinephrin output is totally suppressed. Fatal adrenal insufficiency is produced in animals in all probability by interference with the cortex. Diminished epinephrin output is not an important part of adrenal insufficiency. The suggestion in a quite recent paper (Byrne (53)) that hypertrophy of the adrenal, mainly of the cortex, in soldiers dead from the effects of underfeeding in a German prison camp was compensatory, in order to restore the blood pressure lowered by the want of food, ignores the two fundamental facts, that the epinephrin is given off from the medulla not from the cortex, and that the maintenance of the normal blood pressure does not depend in any important degree upon epinephrin.

Pende (70) speaks of the hypoadrenal constitution as a clinical and pathological entity first studied in Italy (constitutional angihypotony of Ferranini). In reading this paper and many others by "clinical endocrinologists," especially the French and the Italians, the physiologist can scarcely escape the feeling that here he has broken through into an uncanny fourth dimension of medicine, where the familiar canons and methods of scientific criticism are become foolishness, where fact and hypothesis are habitually confounded, and "nothing is but what is not." "In such temperaments (hyperthyroid status more or

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less associated with stigmata of lymphatism or of constitutional hypoadrenalism) 'sympathicotonia' generally prevails and may be associated or alternated with 'vagotonia.'" "In the vagotonic constitutions described by Eppinger and Hess the stress of war frequently leads to frank vagotonia." "People with prevailing 'vagotonic hormones' are liable to a particular type of soldiers' irritable heart of a vagotonic form. In another group of cardiopathies (hypoadrenal types of Satre) in soldiers one is apt to think of hypoadrenalism, and we can accept the hypothesis of a functional inhibition of the adrenals due to the war." "The neuropsychogenic origin of the adrenal insufficiency of these patients, which must obviously come from a certain instability of the glands or from an easy exhaustion of their secretory nerves, explains the peculiar clinical characters of this form and its easy curability by the removal of its psychic causes." There is no evidence of "adrenal insufficiency" in these patients which will stand the test of critical examination for a moment. Nor is it at all obvious that if there is insufficiency, it must come from a certain instability of the glands, on which there are no experimental data, or from an easy exhaustion of their secretory nerves, which hitherto have been only shown to govern the epinephrin output, and which can be completely severed without producing noticeable effects on the health of animals.

Adrenal asystoly (Josué) (71) is the name given to a supposed syndrome in which sudden death from heart failure is apt to occur, associated with the presence of disease or marked diminution in size of the adrenals. There is no real foundation for the view that the heart stops because the adrenals naturally supply a physiological stimulus necessary for its contractions. But it is very probable that if the adrenals are extremely diseased, the profound changes in the metabolism which must be presumed to occur will affect the heart, as well as other organs. The "syndrome of hypoadrenalism described in soldiers suffering from infectious icterus in Italy by Frugoni, Gardeghi, Ancona, Notari and Monti; from typhoid by Frugoni; from dysentery by Izar, Dujarrie, Riviere and Fillerval, and from indefinite infections by Carles and Satre," can scarcely be more at present than the product of an undisciplined imagination.

Anti-typhoid vaccination has also been stated by several writers (Loeper (72), Lian (73), Satre (74)) to cause, sometimes, symptoms of adrenal insufficiency (arterial hypotension, etc.) It is a sufficient commentary on this, that arterial hypotension is not a symptom of adrenal insufficiency experimentally produced, at least not a primary symptom. "The adrenal symptoms in these infections are no doubt accentuated in their initial stages by the capsular exhaustion due to the excessive war fatigue. (Sergent)." There is no experimental exidence whatever that fatigue diminishes the output of epinephrin, and, of course, no evidence that the function of the adrenal cortex, whatever it may be, is diminished in that condition. Until we have such evidence, what is the use of a clinical observer looking at a sick man and saying "No doubt he is suffering from capsular exhaustion due to excessive war fatigue," or to so-called shell shock (Carles) (75)?

Adrenal dyspepsia (Loeper, Beuzard and Wagner (76)), adrenopathic hyperchlorhydrias (Kaplan and Greff (77)), and other digestive disturbances have been described as due to adrenal insufficiency, on no other evidence than that the administration of adrenalin seemed to do good. As has been emphasized repeatedly by physiologists, the pharmacodynamic or therapeutic effects of adrenalin cannot be used to prove the existence of a deficiency in the output of epinephrin. Hoskins (78), for instance, asks very pointedly whether because cascara is efficacious in relieving constipation we ought to conclude that this is because the patient is suffering from hypocascarism?

The diagnosis of "suprarenal" forms of malaria in which adrenal insufficiency is supposed to contribute to the clinical picture (Fraga (79), Paisseau and Lemaire (80), Portocalis (81)) is surely risky on the basis of any physiological knowledge at present at our disposal, although the presence at autopsy of lesions in the suprarenals, described by the last named authors is, of course, well worthy of being recorded. That in one of Fraga's cases the parasite was found in the capillaries of the suprarenal cortex would prove little more than that blood was found there. Similar attempts have been made by not a few writers to establish adrenal insufficiency as one of the factors in the clinical picture in certain groups of cases of

influenza (Cowie and Beaven (82), Ricaldoni (83)). The fact that in diphtheria, typhoid and sometimes typhus the adrenals are sometimes small, and contain little adrenalin and cholesterol (Marañon (84)) would not justify the conclusion, that accidents of the nature of collapse occurring in these and other infections are due to adrenal insufficiency. As already pointed out, it has not been shown that a relatively small epinephrin store means "exhaustion" of the gland and a small epinephrin output. Nor does experimental diminution of the epinephrin output or its total suppression entail any serious consequences.

A large, though quite undeserved place has been occupied in the clinical literature of shock and allied conditions by adrenal insufficiency, or one or other of its aliases. (Loeper and Verpy (85), et al.). There is no evidence that any notable change occurs in the epinephrin output in either direction, or that if it does occur it could play any important part in producing cardiovascular shock (Henderson, Price and Haggard (86), Stewart and Rogoff (87)).

Quite as devoid of experimental basis is the theory supported especially by a number of French writers (88), that in cholera the most characteristic symptoms are due to acute adrenal insufficiency. Luckily, neither in cholera nor in surgical shock does this interfere with the therapeutic use of the drug adrenalin, if that should be indicated on physiological grounds.

Delayed death from burns has been attributed to adrenal insufficiency (Kolisko, Lattes (89)). Adrenal insufficiency has also been advanced as the cause of the prolonged asthenia sometimes seen in aviators after flying at high altitudes (Ferry (90)). Even seasickness has been attributed to hypoadrenalism (Naamé (88)) due to inhibition of the adrenals by the rolling of the ship, also to hyperadrenalism (Cazamian (91)) due to stimulation of the adrenals by the rolling of the ship. Curiously enough, both authors recommend adrenalin in this condition, although the advocate of the theory of hyperadrenalism gives atropin also. It is known that atropin does not diminish the output of epinephrin in the least (Tscheboksaroff (92), Stewart and Rogoff (93)). Mankind can apparently be divided into sheep and goats in regard to this matter, that is to say into sympathicotonics and vagotonics, and the vagotonics have

the better chance of escaping seasickness—if vagotonia (95) and sympathicotonia exist in ordinary, tri-dimensional medicine, and if seasickness is due to hypoadrenalism. But "by my troth, Captain," as Mrs. Quickly has it, "these are very bitter words," for the physiologist or the experimental pathologist—these words like vagotonia and sympathicotonia, hypo- and hyperadrenalism, hypo- and hyperadrenalinemia and all their cousins and connections. For he knows that in most cases they are but words, and in science words which conceal or even distort the facts do not leave a sweet savor in the mouth.

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THE MICROSCOPIC APPEARANCE OF TWO TESTES NINE MONTHS FOLLOWING UNILATERAL VASECTOMY.

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In 1915, while studying the effects of castration on the vasomotor responses to nicotine (1), two dogs were standardized to this drug and the right vas occluded and resected. The two animals, A and B, were in excellent condition and weighed 9.5 and 10 kilos respectively. The operations were done in February, and the animals permitted to survive until the following November, at which time their weight was A, 11.5, and B, 13 kilos. The vascular response was again determined and the results of the previous operations carefully examined. The blood pressure readings gave figures practically the same as those obtained nine months previously. In each dog the stump of the resected vas was found bound down by masses of connective-tissue. Bulging of the vas was not present. However, upon opening the lumen of the stump connecting the testis a small amount of fluid material escaped. This fluid was examined microscopically but no living sperm were demonstrable although much cellular material and debris was present. The testis of the unoperated vas was found firm and normal in appearance. On the other hand, the gland of the occluded vas (occlusion determined microscopically) was smaller than its mate and easily compressible.

Histological examination of the glands on the operated side showed them to be in a very much better condition than was anticipated. The seminiferous tubules, although showing the results of destructive processes, contained much spermatic tissue. In many of the tubules sperm heads were readily identified; in places spermatids were seen. The interstitial tissue in each of the two glands seemed to be somewhat in-

creased. The left glands appeared entirely normal and did not show an increase in the interstitial tissue (cells of Leydig).

Until recently it has been pretty generally believed that complete occlusion of the vas results in the ultimate disappearance of the spermatic tissue and an increase or hypertrophy of the interstitial cells. However, the studies of Steinach (2) and the recent results of Kuntz (3) indicate that if degeneration does occur in the spermatic tissue following vasectomy that such changes are probably not permanent. One of Kuntz's dogs which was permitted to run a period of 140 days following vasectomy, showed a practically normal testis. However, other animals of his series which were permitted to survive shorter periods of time did show varying degrees of degeneration of the spermatic tissue and hyperplasia and hypertrophy of the interstitial tissue.

Alterations in the physical and psychical signs of sex did not occur in the two dogs here reported, during the period of observation.

Therefore, unilaterial vasectomy does not appear to alter vascular responses to nicotine, to bring about alterations in the characters of sex, nor to determine complete disappearance of the spermatic cells from the seminiferous tubules as late as nine months following the operation.

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THE INTERNAL SECRETION OF SANDSTROEM'S GLANDS. PARATHYROID HYPOFUNCTION AND ECLAMPSIA

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In 1896, Vassale and Generali (1) demonstrated experimentally that the parathyroids, which were discovered in 1890 by Sandstroem, and which were believed to be an embryonic residue of the thyroid, are indispensable to life, the abolition of their function causing death from tetany. Afterwards Massaglia (2) completed this study. Operating on puppies, he was able to remove the thyroid without disturbing the two external parathyroids (sometimes in the dog these glands are situated at the anterior poles of the thyroid). In these experiments the animal later developed myxedema, but never developed tetany. In the litter control the removal of both the external and one of the internal parathyroids produced no morbid symptoms, and the animal remained normal. The experiment shows clearly that the thyroid and Sandstroem's glands have different functions. The former exerts a trophic action on the metabolic changes of the body; when this function is abolished, myxedema follows. The latter exercise an antitoxic action; when this is abolished, fatal tetany is the result. Eiselsberg (3), before Massaglia, was able to produce myxedema in lambs and in goats; but this experiment did not show the functional independence of the two glands. In herbivorous animals, Sandstroem's glands are situated some distance from the thyroid; consequently Eiselsberg, without knowing it, failed to remove the parathyroids, as Massaglia did purposely in his experiments with dogs.

These findings have proven useful to the surgeon; from them the explanation of post-operative tetany is given; and they have shown that some parathyroid tissue must be left *in situ.* that tetany may not develop. Vassale (4) and Massaglia (5) later continued the study of the function of the parathyroids, and were able to demonstrate that this tissue neutralizes

the toxins arising from pregnancy and muscular fatigue. This study gave rise to the hypothesis that a hypofunction of the parathyroids can produce eclampsia. Massaglia and Sparapani found, moreover, that the eclampsia of animals is similar to the experimental tetany which occurs in the female dog during pregnancy, when there is a parathyroid hypofunction.

These data were supported by some authors [Zanfrognini (6), Pepere (7), Vicarelli (8), etc.] but were contradicted by others [Haberfeld (9), Soli (10), etc.]. Finally Massaglia (11) answered:

"Die experimentelle Tetanie, welche nach der teilweisen Parathyroidectomie die Weibchen gewisser Tiergattungen während der Schwangerschaft und Stillung befällt, bietet, wenn man von einigen Unterschieden absiehr, bezüglich dere man die verschiedene zoologische Art berücksichtigen muss, ohne Zweifel ein egewisse Aehnlichkeit mit der Eklampsie der Frauen dar. Die negativen Befund einiger Autoren—kann man,—durch die Annahme erklären, dass die parathyroidale Insuffisenz nicht immer als einsiger Faktor wirke und kein zur Herbeifuhung jenes Zustandes der Autointoxication, welcher das Komplexe, vielgestaltige und schwere Krankheitsbild des eklamptischen Anfalles erzeugt, immer notwendiger Faktor sei."

Since the problem had not been completely solved, it seemed worth while to investigate the matter further and the following studies were made:

A.—The 1st series of the studies treats of the consequences of parathyroid hypofunction in cats and dogs during pregnancy. Twelve experiments were carried out, since eclampsia in women does not always manifest the same symptoms, and since it was hoped to reproduce experimentally several of the various syndromes of this malady, and also to see if it were possible to obtain the same general rules governing the moment of the onset of the malady, its clinical course, its issue, and the consequences incident to delivery, so that a comparison with cases of eclampsia in women could be made. Of these twelve experiments, some have already been published. To these is added a case of eclampsia in a female dog, which was studied with Dr. Sparapani. [Massaglia and Sparapani (5).] Both the external and one of the two internal parathyroids were removed from the experimental animals. Under normal conditions the animals show no morbid symptoms after the operation, except at times a very slight albuminuria. This special state of hypofunction is designated as "latent parathyroid insufficiency," because the remaining parathyroid is able to carry on the para-

thyroid function. When there is an increase in the toxins which normally is neutralized by these glands, the single parathyroid then becomes unable to meet the demand, intoxication ensues, ending in tetany. Evidence that intoxication is not normally present in latent parathyroid insufficiency is given by the fact that when the skull is trephined and a slight irritation of the Rolandic area is caused, we obviate the occurrence of tetany; for the toxic substances which are neutralized by the parathyroids would otherwise exercise their action in the neuraxis.

When the internal parathyroid in dogs were not found, one of the two thyroid lobules was removed, or only the two external parathyroids were extirpated.

B.—The 2nd series embraces 11 experiments in which a state of latent parathyroid insufficiency was associated with renal hypofunction, in order to determine whether a functional correlation exists between these organs, and if some toxic substances not neutralized by the kidneys can cause tetany because of parathyroid insufficiency.

C.—The 3rd series consists of 8 experiments in which an endeavor was made to ascertain whether the parathyroids neutralize the intestinal toxins.

D.—The 4th series embraces 8 experiments, in which the problematic functional correlation between the liver and the parathyroids was studied.

E.—The 5th series of 4 experiments has already been published in part. In these experiments it was shown that the parathyroids neutralize the poisons of fatigue.

F.—The 6th series consists of only 2 experiments, because I failed to secure the desired results. In these an endeavor was made to ascertain whether lead poisoning in conjunction with parathyroid hypofunction causes tetany in animals.

SERIES A.

Tetany in pregnancy and in the first days after delivery caused by parathyroid hypofunction.

The symptoms of tetania parathyreopriva have been so thoroughly discussed by others that no repetition is necessary. The diet of the animals in these experiments was bread and meat; during the tetany they refused food, but were always thirsty. They were given water and milk. For treatment, para-

thyroidin with calcium chloride was used. Sometimes it was not possible to make a microscopic examination of the urine. Twelve female dogs were used and the parathyroids were removed as described. The results of the experiments indicate that the disorders produced have the following points in common with eclampsia:

1.—The animal, after the removal of three parathyroids, continues in good health, providing that it lives in normal conditions. When it becomes pregnant it shows tetany. What is true of the animal applies to woman also, viz.: that while one would not ordinarily expect illness for her, yet she may have eclampsia in pregnancy.

2.—The first indication of the coming attack in women and in my animals, is albuminuria, very light in the beginning. We rarely have an exception to this rule in women or in animals.

3.—The tetanic attack, as does eclampsia, has the prodromata,—some slight symptoms of tetany. Both occur, generally, at the end of pregnancy or during the puerperium. When we have any exception in this rule, it is due to some change from normal life, as dietetic errors, or complications.

4.—Various authors recognize several forms of eclampsia. I believe that I have reproduced in my experiments almost all the pictures of this disease.

5.—The daily amount of urine, its abnormal components, especially albumin, before, during, and after the tetany were the same in my animals as in eclamptic women.

6.—De Lee (12), speaking of the prognosis in eclampsia, says: "Over 20 per cent of women affected with eclampsia die . . . ," and afterwards " . . . for the child the chances are not good, nearly one-half of the children dying." In these experiments almost the same results were obtained, both for the mothers and for the puppies.

7.—In the animals that die, there was found lesions in the liver and in the kidneys. The severity of the lesions varied in the different cases; at times the greatest injury was sustained by the liver, and at times by the kidneys. Several authors have described lesions, especially in the liver, more severe than those I have seen; but we have also cases of eclamptic women which show almost no severe lesions in the kidneys or in the liver.

8.—The meat diet, in these animals, as in women threatened with eclampsia, seemed to favor the onset of the attack; on the contrary, milk seemed to have a preventive and curative action against tetany.

9.—The treatment with parathyroidin and calcium salts gave good results; indeed, the animals died almost always during the night when it was not possible to administrate the treatment. Since the toxin of tetany injures the central nervous system [Uhlenhuth (13)], it is imperative that the treatment be instituted without delay.

10.—The tetany that was caused in these experiments is similar to the eclampsia of animals. Veterinarians [Saint-Cyr e Violet (14), Delmer (15)], have concluded that this condition in animals is the same as eclampsia in women. In a case (female dog), observed by me with Dr. Sparapani [Massaglia (5)], I reached the same conclusion. This fact makes more certain the deductions from the results of the experiments.

SERIES B

Study of the relation between the renal and the parathyroid function.

When a pregnant animal in a state of latent parathyroid insufficiency is affected with tetany, it shows a disturbance in the renal function during the attack, and sometimes before and after the attack. From these data I have endeavored to prove what functional correlation exists between the kidneys and the parathyroids, and also what part the kidneys play in the genesis of eclampsia by parathyroid hypofunction. Therefore, in the experiments in this series I have associated with a parathyroid hypofunction, stenosis of the ureters (5 experiments), stenosis of the renal veins (5 experiments), and stenosis of both renal veins and ureters (1 experiment). Dogs were used as the experimental animals and the parathyroids were removed as previously described.

The results of the series showed that renal hypofunction does not cause the parathyroid hypofunction. When the kidney function in the animal was severely impaired, uremia and death were caused—not tetany. It is true that sometimes it is impossible clinically to distinguish between a case of tetany and a case of uremia with convulsions; but the diagnosis becomes easy enough when it is made on several cases in which it

is possible to follow the course of the disease from the beginning to the end.

A.—As a matter of fact, in the animals of this series, the nervous symptoms sometimes appeared and sometimes did not, just as occurs in uremic intoxication. In intoxication from parathyroid hypofunction, however, the predominant symptoms are always neural.

B.—The nervous symptoms usually developed when the renal function was almost abolished—that is to say, just before the death of the animal.

C.—In these experiments, when the nervous symptoms appeared, they did not give the classic picture of tetany by parathyroid hypofunction.

Now, how can we explain the fact that a renal hypofunction does not directly produce parathyroid hypofunction when, on the contrary, the hypofunction of these latter cause trouble in the function of the kidneys?

The kidneys, as we know, together with the skin, the lungs, and the intestines, exercise the function of eliminating from the circulation the waste materials which have passed all catabolic transformation necessary for them to be excreted. When the renal glands are injured, we have in the circulation a retention of these waste materials; intoxication results, which finally, if severe, causes uremia. [Wells, (16)]. This intoxication can produce lesions in the parathyroids, as in the other organs (lesions were found with some frequency in the liver, in the intestine, etc.), [Dieulafoy (17)], but can not directly produce a parathyroid hypofunction, because the waste materials which remain in the circulation are materials which have undergone every modification necessary to their being excreted, and they probably contain also the poisons formerly modified by the parathyroid secretion.

On the other hand, the parathyroid glands neutralize certain catabolic substances. When these are not neutralized and reach the kidneys, these glands are injured, because the unmodified substances are not able to be excreted. Consequently we have a special intoxication, which, when severe, exercises its action on the nervous system and causes tetany.

SERIES C

Parathyroid function and intestinal toxins

Many disease conditions, such as headache, malaise, lassitude, tetany, epilepsy, and eclampsia, are attributed by some authors to poison of gastro-intestinal origin. This fact is not demonstrated; however, it would seem that toxic substances from the intestine increase the severity of any of the above morbid conditions. [Wells (16)].

The intestinal poisons are augmented by the retention of the intestinal contents, which cause an excessive intestinal putrefaction. Tissier (18), Metchnikoff with his pupils in the "Institute Pasteur," and several other authors have demonstrated that the bacteria of the "flora intestinalis" change in number and in species, according to the ingestion of the different foods; consequently the intestinal poisons change also.

In view of these data, and inasmuch as the observations from the experiments of Series A show that, in the case of animals in a state of latent parathyroid hypofunction and in pregnancy, a meat diet precipitates and increases the violence of the tetanic attack, while a milk diet weakens, if it does not entirely obviate it, I was led to investigate whether the parathyroids exercise some action upon the poisons which enter the circulation from the intestine. Therefore the normal function of the intestine was altered, either by producing intestinal stenosis or by feeding the animal great amounts of meat, or cultures of microbes from the "flora intestinalis."

Five experiments were made with stenosis of the intestine, and three with ingestion of great quantities of meat or of cultures of bacteria from the "flora intestinalis." The normal diet of the animals under experimentation was bread and meat. Cats and dogs were used and the parathyoids removed as previously described. In some of the animals, in a state of latent parathyroid hypofunction, I abolished the external pancreatic secretion by ligature and resection of the pancreatic ducts. A normal diet of bread and meat did not cause any symptoms of tetany.

The results of this series showed that, taken together with those of series A, a derangement (especially when the animal is fed on flesh) in the function of the intestine which produces an increase of the toxins, either by stenosis or by the ingestion

of a large quantity of germs or meat, causes tetanic symptoms in an animal in a state of latent parathyroid hypofunction; viz., that the insufficiency from being latent becomes apparent, and from this it is concluded that the parathyroids neutralize some intestinal poisons, especially those which come from a meat diet.

In some animals in a state of latent parathyroid hypofunction, I abolished the external pancreatic secretion by ligature and resection of the pancreatic ducts. A normal diet of bread and meat did not cause any symptoms of tetany.

SERIES D

The antitoxic function of the liver in relation to the antitoxic function of the parathyroids.

It seems that all, or a great part of the protein absorbed by the intestine reaches the liver by means of the capillaries; likewise the toxic substances are carried to the hepatic gland for neutralization. To these poisons, indeed, we attribute many cases of non-alcoholic cirrhosis of the liver and of acute yellow atrophy of the liver when of idiopathic origin. [Wells (16)].

Hahn, Massen, Nencki, Pawlow (1892), as reported by Luciani (19), studied the antitoxic function of the liver by means of Eck's fistula in dogs. In the few animals which survived the operation, these authors observed, after about ten days, some tonic-clonic convulsions followed by coma. These attacks followed the eating of a great amount of meat and the intoxication was caused by ammonium carbamate, which is probably an important precursor of urea and which in dogs with Eck's fistula could not be converted into urea. The ammonium carbamate, indeed, being a substance of considerable toxicity, is considered, when free in the blood, an important factor in the production of uremic symptoms. The liver normally decomposes carbamic acid into water, carbonic acid, and urea. In the animal dead from Eck's fistula, the liver showed atrophy and fatty degeneration Furthermore, later the studies of Bisso (1895) [see Luciani (19)] demonstrated by a method of progressive stenosis of the portal vein that the liver destroys the toxic substances which come from the intestine and, when the function of the liver is impaired, the kidney suffers. Therefore there exists an indirect functional relation between these organs. From these data, and having found lesions in the liver

in my animals dead from tetany caused by parathyroid hypofunction during pregnancy, it was thought that, although in hepatic diseases which produces atrophy of the gland we do not usually have convulsive symptoms, it would be useful to study the consequences of the association of a parathyroid hypofunction with hypofunction of the liver.

Two methods were used in producing hypofunction of the liver:

A.—Progressive stenosis either of the common bile-duct or of the portal vein.

B.—By producing a severe lesion in the gland. As a matter of fact it is known that with phosphorus poisoning we obtain lesions similar to acute yellow atrophy of the liver, the same lesions that are sometimes found in cases of eclampsia. Orth (20), Giacosa (21).

The normal diet of the experimental animals was bread and milk.

The results of these experiments lead to the conclusion that the hypofunction of the liver which follows stenosis either of the common bile duct or of the portal vein (a method which offers some difficulty), or poisoning with phosphorus, associated also with a state of latent parathyroid insufficiency, does not usually cause symptoms of tetany.

Hahn, Massen, Nencki, and Pawlow obtained tonic-clonic convulsions in the few dogs surviving the operation of Eck's fistula. But in these animals the hepatic function was abolished, and the convulsive symptoms developed after a heavy meat diet and when the dogs were about to fall into a state of coma. Considering these data and those I obtained from the experiments of this series and those of Series A and C, I conclude that the liver neutralizes the poisons which, after a meat diet, enter into the circulation from the intestine, and that the parathyroid glands probably help the liver in this important function.

SERIES E

The muscular fatigue in dogs in a state of parathyroid hypofunction.

In 1906 Massaglia (5) demonstrated by means of experiments on dogs that the toxins of muscular fatigue are neutralized by the parathyroids. When the parathyroids are insuf-

ficient to carry on their function, we have albuminaria in the animal, and, if the parathyroid hypofunction becomes more pronounced, we have symtoms of tetany. In that series of experiments dogs were made to run in a treadmill for various periods of time until partial or complete muscular exhaustion was produced. The results of the studies demonstrated that the parathyroids have the function of neutralizing the poisons of muscular fatigue. We know that in pregnancy the muscular fatigue is great during labor, and that it is greater in primaparae than in multiparae.

The experiments wherein exhaustive muscular activity in the dogs was produced demonstrate: 1.—That the parathyroids have the function of neutralizing the poisons of muscular fatigue. We know that in pregnancy the muscular fatigue is great during labor, and that it is greater in primiparae than in multiparae. De Lee (12) says: "Primiparae are affected by eclampsia oftener (3 to 1) than multiparae, and in about 20 per cent of the cases the convulsions begin during pregnancy, in 60 per cent during labor, and in 20 per cent after delivery." In the animals of the experiments of Series A, tetany was more frequent during labor than in any other period. Also at the end of pregnancy, the organs which exercise the antitoxic function (among them the parathyroids, with a vital function) have a heavy burden on account of the great increase of waste products. A sudden appearance of the poisons of muscular fatigue in the circulation as a consequence of labor can easily determine a parathyroid hypofunction with all its consequences.

The kidneys also suffer from a parathyroid hypofunction. If the renal hypofunction has no direct action on the function of the parathyroids (experiments of Series B), parathyroid hypofunction, on the contrary, has a direct injurious action upon the kidneys. This fact explains: A.—Why, in pregnancy, at the beginning of a parathyroid hypofunction, one of the first alarming symptoms is albuminuria. B.—Why sometimes in a state of latent parathyroid insufficiency, and with good health, we have faint traces of albumin in the urine. The only internal parathyroid which remains is not always able, even in normal conditions, to accomplish its function completely.

SERIES F

Lead poisoning in animals in a state of latent parathyroid hypofunction.

As we all know, lead poisoning causes lesions in the liver, in the kidneys, and in the nervous system. Among the morbid symptoms accompanying saturnism, we have many nervous troubles, with sometimes a true convulsive form. [Dieulafoy (17)]. Therefore I tried to prove whether lead poisoning in an animal in a state of parathyroid hypofunction would cause tetany. Two dogs were poisoned slowly with sulphate of lead; both animals, after about 6 months of chronic poisoning, died, but without ever showing symptoms of tetany. The studies were not continued since I was convinced that lead poisoning does not produce a parathyroid hypofunction.

DISCUSSION AND CONCLUSIONS

The results of the experiments may be summarized as follows: The parathyroid glands appear to have the function of neutralizing or of breaking down into waste products of simpler chemical composition the complex bodies of catabolic changes, or toxic substances derived from pregnancy and puerperium, from the intestine, and from muscular fatigue. They also demonstrate that an intoxication from a parathyroid hypofunction injures, more or less, the kidneys, the liver, and the nervous system; that there exists between the liver and the parathyroids an indirect functional correlation in neutralizing toxic substances which arise from the intestine. A parathyroid hypofunction in pregnancy or in puerperium is then certainly a pathogenic factor of eclampsia. This factor, as has already been stated, does not exclude other factors in the pathogenesis of eclampsia.

How can we explain the pathogenesis of eclampsia and its different syndromes? We know that uremia is the consequence of the retention in the circulation of waste products of metabolism which have passed through all the catabolic phases necessary for their excretion by the kidneys. A lesion in these glands can cause a retention of these waste products, which, when they exceed a certain amount, cause uremia. [Wells (16)]. The morbid pictures in this condition may differ widely, since there are a number of different catabolic substances which may remain in the circulation, and the resistance of the different or-

gans to these substances is not constant. Eclampsia, on the contrary, is an intoxication due to retention in the circulation of a certain amount of waste products, part of which is derived from the common metabolism, and part from the fetus and the placenta. [Wells (16)]. I wish to emphasize here, however, in view of what I shall later prove, that the symptoms of the eclamptic attack are similar to those of a uremic attack in the cerebral form of uremia. Indeed, it is possible to differenitate between the two conditions only through the etiology of the case, and from the fact that (if the woman does not die) with the issue, because, overcoming the eclampsia, the kidneys, as a rule, become normal again; on the contrary after the uremic attack nephritis generally remains.

Why do these waste products remain in the circulation? The data which I have gathered from my experiments, in which I reproduced a syndrome entirely similar to eclampsia, induced me to formulate the following theory: In pregnancy and in puerperium we have an increase of the waste products in consequence of an increase of the metabolic changes; this is in addition to the waste products derived from the fetus and the placenta. The result is the added work for these organs which normally keep the body free of these catabolic substances. The parathyroids have the function of neutralizing some or all of the waste products and the poisons derived from the fetus, the placenta and from the muscular fatigue—this is great during labor—and also in part from the intestine. Very frequently there are troubles in the intestinal function during pregnancy. If the parathyroids are not able to carry on their function, we have in the circulation some metabolites not converted into products which could be eliminated normally in the urine. These produce in the liver, in the kidneys, in the nervous system, and in other organs, lesions more or less severe, the degree of severity depending upon their nature and extent and the resistanc of the organs affected. The organs which normally keep the body free of waste products are able, for a time to eliminate them from the circulation, but finally, because of injury, they are no longer able to accomplish this, and we have a severe intoxication, and, in the end, an eclamptic attack.

But what special part have the kidneys and the liver in the pathogenesis of eclampsia? Normally, the kidneys have the

function of eliminating many converted catabolic products. In pregnancy and in puerperium the renal glands eliminate these in an increased quantity, together with some waste products from the placenta and the fetus. If we have parathyroid hypofunction, the waste products not converted by the parathyroid secretion go to the kidneys, which, for a time, eliminate them also (indirect functional compensation). But these catabolic substances easily injure the renal glands. As pregnancy advances, the catabolic substances in the circulation increase, and consequently the parathyroid hypofunction increases also; then the lesions in the kidneys become more severe. The time comes when these poisons can not be eliminated from the body. It is at this time that the very dangerous intoxication arises as a result of the retention of catabolic products not converted by the parathyroids and of an increase in the common catabolic substances which are normally eliminated by the kidneys. Eclampsia is the final result of this condition. My conception explains the cases in which we have marked anuria before the eclamptic attack as well as the autopsy findings of severe lesions in the kidneys. Therefore renal hypofunction is a very important factor in eclampsia resulting from parathyroid hypofunction.

But the kidneys may sometimes be the primary factor in eclampsia. The great burden of eliminating the waste products (perhaps some trouble in the circulation of the gland, or a compression of the ureters) can cause injury to the kidneys, or make it easier for one to become ill from exposure to cold, from some flagrant error in the diet, or with some infectious disease. One develops, in this case, an acute nephritis with convulsions. [De Lee (12)]. Clinically, we can not differentiate these symptoms from those of cerebral uremia, but we call this condition eclampsia, and not uremia, because it is caused principally by intoxication from the waste products of pregnancy. Indeed, when the uterus is emptied of its contents, rapid improvement often follows. This does not occur in common nephritis, and the lesions in the kidneys are often accompanied by lesions in the liver.

It now seems certain that the hepatic gland has the function of neutralizing poisons. To the action of these poisons several authors [Wells (16)] attribute some severe lesions of

the liver, as acute yellow atrophy and non-alcoholic cirrhosis. Now, when we recall that in pregnancy the intestinal poisons are often greatly increased, since intestinal troubles are very common in this condition [De Lee (12)], that there are in the circulation many waste products from the material change, and that the liver very easily suffers from renal and parathyroid hypofunction, we find the reason why the hepatic gland is so often injured in eclampsia, and also an explanation of the nature of the lesions it sustains. [Orth (20)]. Then the liver is a secondary, but a very important and frequent factor in the pathogenesis of eclampsia.

But some of the causes cited above may cause lesions in the liver before any other organs. In this case the hepatic hypofunction may become the primary factor in eclampsia. As a consequence of hepatic hypofunction, we have in the circulation some amino-acids, not converted into urea, which have a toxic action, some intestinal poisons, and probably other products not neutralized by the liver. These poisons exercise an injurious action, especially upon the nervous system and on the kidneys, causing a dangerous hypofunction of these organs; finally, they may also determine a hypofunction of the parathyroids, which are overworked at this time in neutralizing many other catabolic products. The final consequence of this intoxication is eclampsia. These are probably the eclamptic cases [De Lee (12)] in which the patient has, among other symptoms, jaundice, petechiae, and, in case of death, very severe lesions in the liver.

Treatment—De Lee (12) says of eclampsia: "One can speak of rational prophylaxis only when the cause of disease is known. Since we do not know the cause of eclampsia, our treatment is all empiric."

These studies have, I hope, thrown some light upon the causes of eclampsia. It is necessary, after the diagnosis is made, to discover what organ has yielded first in its antitoxic function, and so to determine the nature of the poisons causing the intoxication. Then it is possible to obtain good results by instituting an immediate antitoxic treatment with special reference to the organs first affected. I know that this etiologic diagnosis is not easy to establish, especially when the attack occurs almost without warning. But eclampsia is most often

caused by a parathyroid hypofunction, and, for this reason I believe it wise always to use the opotherapic treatment (parathyroidin). Moreover, this treatment should be instituted before the appearance of any strong convulsive symptoms, because, as I have said, when the nervous system is severely injured, it recovers with great difficulty. When medical treatment is without effect, it is the part of the obstetrician to determine when it is time for emptying the uterus.

I wish to thank Professor F. C. Becht for assistance and advice in my work.

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HYPOPITUITARISM—FROEHLICH TYPE

In an Infant—Nine Month's Old

M. BOYD KAY

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Baby J. S.—Age, nine months; weight, twenty-one pounds, was admitted to the Out-Patient Department of the Children's Free Hospital, July 29th, 1920, the mother seeking medical advice because the neighbors had told her that her child was "crazy." This opinion was based upon the facial aspect of the baby, which was that of marked stupidity.

The family history is not remarkable except for the fact that the mother has had two miscarriages, one at the third month, and one at the fourth month of pregnancy. No case of mental deficiency has occurred in either branch of the family; the one other living child being quite normal.

The child herewith reported was a full term baby; delivery was easy; weighed seven pounds and was entirely healthy at birth. It has always been breast fed and has suffered from no acute illnesses. Development was apparently in no way remarkable until the third month, at which time it was noticed that the weight began to increase rapidly. The mother also noticed that from this time on the mentality of the child was regressing; its stupidity becoming more and more pronounced. Sleep was almost continuous, and the waking moments were devoted almost entirely to feeding. The child did not sit up until the eighth month and at the ninth would not sit alone, and supported his head with difficulty. The feedings are taken quite well and there is a mild constipation. A very marked polyuria is present, the mother stating that she cannot keep the child dry. (I have recently seen a child with a glandular dystrophy that passes its urine almost continuously, the act being involuntary, though the child has passed the age of incontinence. The enormous polydypsia which accompanied this condition was the interesting factor. The child, though less

than two years old, drank three quarts of milk daily, besides water in a like quantity, as far as I can figure from the parents' statements. In all about six quarts of fluid were consumed daily.)

EXAMINATION: A very stupid appearing child; the skin is uniformly clear, warm, moist and velvety; the general appearance is that of a very fat child, of the Fröhlich type, with the characteristic enormous abdomen and thighs.

HEAD: The circumference is 18.5 inches; the hair is scanty and soft. The eyes show an evident divergent squint and there is a slight nystagmus. The tongue is continuously protruded from the mouth (this is not macroglossia) and a constant dribbling of saliva is evident. There are no teeth. Nothing noteworthy is found in the throat.

CHEST: Very fat, but in no way remarkable, except for the presence of a large thymus gland; the heart and lungs reveal no adventitous sounds. The circumference of chest is twenty inches.

ABDOMEN: This is of interest on account of the distribution of the sub-cutaneous fat. Although the entire abdomen is quite fat it is found that the greatest distribution lies below the level of the umbilicus; here the circumference is twenty-two inches . The abdominal organs are found to be in no way remarkable.

EXTERNAL GENITALIA: They are exceedingly small. Upon first inspection the impression is given that the penis is buried in the excessive fat, but upon trying to express the organ only a rudimentary condition is found to be present. The testicles are also quite small.

HIPS: Ponderous; their circumference is 22.5 inches.

EXTREMITIES: The arms are quite fat, the hands are broad, the fingers, tapering though not unusually short. The legs are very fat; the thighs measure fourteen inches in circumference.

OPHTHALMOSCOPIC EXAMINATION: Pale disc, but not atrophic; the muscular regions are reported as normal.

URINE AND BLOOD EXAMINATIONS: Normal.

TEMPERATURE: Though a uniformly subnormal temperature might be expected in this condition, only once was the rectal temperature below 98° F. On one occasion following the injection of one mil of antuitrin, it rose to 100° F., after twenty-four hours.

CARBOHYDRATE TOLERANCE: This was quite high, as shown by the following observation: In addition to other foods, the child received daily for three successive days, 150 grams of cane sugar. A specimen of urine obtained at the end of this period and on successive days, failed to reduce Fehling's solution. (The blood sugar was not determined because the mother would not allow the withdrawal of a specimen of blood.)

TREATMENT AND PROGRESS: Treatment was started with thyroid extract (P. D. & Co.) one quarter of a grain, three times a day, whereupon the polyuria immediately disappeared, the protrusion of the tongue ceased, and the dribbling of saliva stopped. The thyroid treatment was gradually increased in amount and very shortly pituitary (whole gland) was added in increasing dosage, until at the present time, the child is taking 3 grains of thyroid extract and 9 grains of pituitary extract daily. The effect of the treatment has been interesting. Almost immediately the somnolence decreased, the mental condition improved, and the child now notices objects and will reach for them. He can at this time (Dec., 1920) stand by holding on to a chair. The weight remains constant. The rudimentary penis has not

shown any evidence of growth, consequently, at some future time, testicular extract will be added to the medication.

COMMENT: The case is reported because as far as I can find it is, I believe, one of the youngest cases of Froehlich type of hypopituitarism to be noted. Though this is undoubtedly a case of poly-glandular dystrophy, particularly of pituitary and thyroid enlargement, I believe the pituitary element to predominate and feel that this theory is borne out by the x-ray photo of the sella turcica. Though the sella is only moderately small a close approximation of the clinoid processes was shown, as is typical in these cases, is particularly marked here. The value of pituitary gland feeding, *per os* has been often questioned. It appears from the course of this case, that such treatment has proven of value.

The presence of brain tumor has been considered but in the absence of outspoken "neighborhood symptoms" such a diagnosis seems doubtful. Time must decide this.

Editorials

THE ADRENALS AND THE EMOTIONS.

A recent article on the James-Lange theory of the emotions in relation to the adrenal glands* suggests that there is still current some misconception regarding the relations of these glands to sympathetic activity. The author says: "Cannon and his collaborators attempted to show that the physical concomitants of fear were produced through psychic stimulation of the adrenal glands." As a matter of fact no such attempt was made, nor was such a belief ever held by the investigator quoted. That strong emotions, pain and asphyxia do cause an augmentation of epinephrin discharge from the suprarenal glands is inherently probable and is supported by many data. Stewart and some other writers, on the other hand, have been unable to convince themselves by direct experimentation that such is the case. In any event, however, the suprarenal discharge cannot be regarded as having any other effect than to augment the action of the sympathetic impulses, the initiation of which precedes the adrenal activity. The fact that only relatively slight effects upon sympathetically innervated structures can be produced either by stimulating the nerves to the suprarenal glands or by direct massage of the glands, and the further fact that under experimental conditions the glands within an hour or two become so exhausted that massage of them is no longer capable of evoking any significant reaction, would seem to indicate that epinephrin discharge plays a relatively minor role in the reactions to emotional stress or pain.

The James-Lange theory postulates that we cannot experience an emotion unless we also experience the physical changes that habitually accompany it. "We are afraid because we run" rather than, as generally believed, "we run

*Kieley, C. E.: James' theory of the emotions in relation to the adrenal glands. J. Lab. & Clin. Med., St. Louis, 1920, 6, 193-194.

because we are afraid." Kieley attempted to put this theory and his misconception of Cannon's theory to the experimental test. To two patients with marked affect disturbances he administered apocodeine over a period of nearly two weeks, with the idea of counteracting or neutralizing the action of the hypothetical excess of circulating epinephrin, and thus doing away with the bodily reactions to which, according to the James-Lange theory, the emotions might be due. The results were negative. The affect disturbances were in no degree ameliorated. The author concludes that, "granting Cannon's contention," the two experiments reported indicate that an emotion can be experienced independent of the physical changes that habitually accompany it.

A striking antithesis of this conclusion can readily be secured by administering 0.5 milligram of epinephrin to a susceptible patient, as is done in making the well-known "Goetsch test." The patients not infrequently develop tremors, pallor, lacrymation—in short, a typical picture of acute emotional distress. But when questioned such patients may state that they are entirely free from any affect reaction, even though they are normally of a somewhat emotional trend. Such observations would seem to afford definite proof that the James-Lange theory is not tenable. —R. G. H.

THE ACTION OF HYPOPHYSEAL EXTRACTS.

It is a matter of common observation that the administration of hypophyseal extracts to one and the same individual or to different individuals not infrequently yields physiological responses of apparently opposite types. Such paradoxical phenomena are more or less disconcerting to the clinician and the investigator alike.

There are at least three possible explanations of these differences in reaction, no one of which can at present be considered as all-sufficient, though a combination of parts of each, may in the last analysis contribute to the interpretation when the data are sufficiently complete.

In a recent article by Parisot and Mathieu (1920) the idea is developed that the differences in the type of response are largely dependent upon the size of the dose employed.

The so-called "dynamogenic" effects are expressed in the results obtained by the use of doses comparable in amount to what the gland itself is supposed to produce during its normal activity, while the "antidynamic" effects appear when doses are applied in amounts which are outside the range of normal glandular productivity. Such a conception suffers from the flaw that we do not know the rate of production of the active principles by the hypophysis. Yet the inherent possibility that the nature of the response is influenced in part by the size of the dose used is entirely valid in many cases.

The second possibility is derived from the observation of Schmidt and May (1917) that by mild hydrolysis of "tethelin" [discovered by Robertson (1916)]—the alleged active principle of the anterior lobe—there is obtained a solution which exerts the oxytocic and pressor effects commonly attributed to posterior lobe extracts, while "tethelin" itself shows no such activity. This finding gives rise to the opinion that perhaps the anterior lobe produces the mother-substance from which the effective principles of the posterior lobe are formed, and that the varied reactions obtained by these latter extracts are due to the predominance of one or another of the compounds resulting in the progress of the transformation, and represent either different degrees or different types of change of the mother substance. Confirmation of this idea must await the chemical isolation, identification and testing of the active principles.

A third possibility is that the physiological status of the subject with regard to the condition of tone of the responsive mechanism at the moment of the application of the extract, is an important factor governing the type of response that will be elicited. There is no reason to expect that, for example, a given blood vessel which is in a condition of constriction will respond to a certain amount of hypophyseal extract with the same type of reaction as will the same vessel to the same dose when it is in a state of relaxation. There is ample experimental evidence supporting this view which if substantiated by further studies is capable of application in principle to the interpretation of the opposite effects produced by the administration of many other substances.

These three possibilities then, the differences in the size of the dose representing differences in the amounts of active principle; the presence in the extracts of differently acting substances in different relative amounts; and differences in the physiological condition of the subject at the time of the administration of the extract, serve as indices for the interpretation of the paradoxical effects obtained. Whether or not any one of them is sufficient to alone explain the phenomena or whether the principles of all must be used is obviously a matter that can only be determined by further exact studies, and it would seem as if the most promising field for such work lies in the determination of the chemical nature and constitution of the active principles of the extracts. —F. S. H.

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Book Reviews

THE ENDOCRINES. By Samuel Wyllis Bandler. Phila. & Lond., 1921. W. B. Saunders Co. 486 p. 8°.

The book comprises mostly a reprint of a series of articles which the author has previously published separately. In addition there are final chapters on "clinics" and illustrative cases. Most of the subject matter has been presented in abstract form in previous issues of this Journal and hence calls for no extensive review.

The book as a whole comprises an interesting exposition of the beliefs which have led the author to the practice of employing endocrine products either exclusively or in part in ninety per cent of the prescriptions he writes.

The matter is presented in a way that renders impossible an impersonal evaluation of its significance. It is, in short, an expanded testimonial based upon personal experience. As such it inevitably raises the question as to the author's competence as a diagnostician and therapeutist. To those who believe the author a master the book will appear a highly significant addition to the literature. On the other hand, there is nothing in the presentation to exclude the judgment that he is merely a deluded enthusiast. The reviewer has no definite information upon the point.

This is said with no invidious intention. The same may be said of other books on so-called practical endocrinology. So far as the reviewer is aware such books without exception are based upon inadequate physiological conceptions. This is necessarily so since endocrine physiology is still in a nebulous condition. Nothing is to be gained, however, by selecting more or less random data to bolster up preconceived theories and ignoring such as are inconvenient. Much would be gained if writers in this field would accept the obvious fact that our fundamental data are in a state of chaos and present their material on a frankly, empirical, statistical basis.

Irrespective of our ignorance of the physiology of the placenta or the mammary glands, for instance, their exhibition as therapeutic agents may or many not be valuable. Bandler insistently states that they are valuable. Most therapeutists doubt or deny this. The matter can be determined in only one

way and that the way by which all therapeutic claims must be substantiated or disproved, namely by scientific investigation. They must be administered under controlled conditions to a large number of patients and the outcome honestly considered with adequate regard to negative as well as positive results. Especially, the element of suggestion must be rigidly excluded. To carry conviction the results must finally be presented for what they are, namely, a body of statistics, with due regard to the canons of statistical science.

That this offers a difficult task is obvious. Until it is accomplished, however, endocrinology can lay no convincing claim to serious regard as a valid science. In the meanwhile the field inevitably will continue to offer a happy hunting ground for quacks and faddists. For this reason, the reviewer ventures to hope that the author of The Endocrines will soon find time to reduce his extensive experience to an impersonal body of observed facts and present it as formal evidence, the lack of which we must all deplore.—R. G. H.

NEUE BEITRÄGE ZUR KENNTNIS DER LANGERHANSSCHEN INSELN IN MENSCHLICHEN PANKREAS. Seyfarth (C.), Jena, 1920, 104 p.

This is a highly important study. First of all much valuable material on the embryology of the pancreas is given. It is stated that the islets of Langerhans develop from the primary pancreatic ducts. Not only during fetal life, but also after birth and even in adult life new islets are continually formed out of the small excretory ducts. These questions have been studied not only in normal organs, but also in the pancreas of syphilitic fetuses and children. Under normal circumstances there, capsules do not exist around the islets. When a capsule is observed it consists of the connective tissue between the acini and does not form a true capsule. The islets are not organs with a special function. They form simply a part of the secreting parenchyma. Therefore, the theory that diabetes has a special connection with the islets is rejected by the author. All diseases of the blood vessels of the pancreas, but especially arteriosclerosis, may cause diabetes. Other causes affecting the pancreas and causing diabetes are alcoholism, syphilis, tuberculosis. Also other infections may produce changes in the pancreas and consequently diabetes. These are only a very few facts taken from this book, which may be most warmly recommended to all workers in the field of diabetes. Six splendid plates increase the value of this study.—J. K.

DIAGNOSTIC UND ERNAHRUNGSBEHANDLUNG DER ZUCKERKRANKHEIT IN DER PRAXIS. (Diagnosis and dietetic treatment of diabetes in medical practice). Schall (H.), Leipzig, 1921, p. 70.

This little book is perhaps the least successful one on this subject in existence. The chemical methods given for the determination of acetone, diacetic acid and β oxy-butyric acid are simply ridiculous. If an investigator wishes to carry out this kind of work he should do it properly; otherwise, he had better not try it at all. The author seems never to have heard of treatment with alimentary rest. Allen, Joslin, Leyton, and others seem to be perfectly unknown to Schall. It is not necessary to give further evidence that this book is superficial and useless. It does not speak well for the medical profession that it is already in the second edition.—J. K.

Abstract Department

(ADRENAL) Clinical notes upon suprarenal insufficiency. Babonneix (L.), Monde méd. (Par.), 1917, **27**, 167-71; Midland, M. J. (Birmingham), 1917, **16**, 129-132.

A brief report of a patient who died suddenly following recovery from acute tonsilitis. The autopsy showed complete destruction of the adrenals. The author assigns two essential functions to these glands—angiotonic and antitoxic; the former maintains the blood pressure at a certain level by adrenine, a product of the medullary substance. The latter neutralizes toxins by the lecithin produced by the cortical layer. Adrenal insufficiency results, therefore, on the one hand in circulatory disturbances—dilatation of the ventricles, acceleration, weakening and irregularity of the heart-beat, small pulse, pallor, white line, syncopal attacks; and on the other hand by an accumulation of undestroyed toxins, with digestive disturbances, anorexia, vomiting, colic, asthenia, etc. The sudden cardiac failures following acute infections like typhoid, diphtheria and scarlet fever, are not due to bulbar intoxication, myocardial disease, neuritis of the vagus, etc., but are purely dependent on adrenal insufficiency. The author agrees with Sergent regarding adrenal encephalitis and considers many so-called neurasthenics examples of adrenal insufficiency and believes chorea due to disease of these glands. Very many cases of sudden death ascribed to aortitis or coronary artery diseases are in reality due to profound changes in the adrenals. Again, most cases of sudden post-operative death or surgical shock are due to the same cause. The "incoercible vomiting" of pregnancy has the same etiology. He is an enthusiastic advocate of prompt adrenal therapy in the above conditions.—H. L.

Blood sugar before and after reduction of the ADRENALS in epilepsy, according to Fischer (Blutzuckerspiegel vor und nach der therapeutischen Nebennieren—"Reduktion" bei Krampfkranken nach Heinr. Fischer). Bausch (W.), Deutsche med. Wchnschr. (Berlin), 1920, **46**, 1353.

The author determined the blood sugar in five patients after extirpation of an adrenal for epilepsy, but found no change. The blood sugar content was always perfectly normal.—J. K.

(ADRENALS) A case of phaeochromocytoma (paraganglioma) of the suprarenals with hypertrophy of the left heart. Bergstrand (Hilding), Hygiea (Stockholm), 1920, **82**, 321-334.

Following a brief description of the types of tumors originating in the suprarenal glands, the author reports a case of paraganglioma of the right suprarenal gland that was discovered at autopsy in the body of a woman, fifty years of age, who died from pneumonia. The tumor was oblong, measuring 5 c.m. x 8 c.m., and weighed 200 grams. It was definitely encapsulated and originated in the medulla of the gland. The tumor was well supplied with atypical blood vessels and had only a small amount of stroma. The tumor cells were packed into a network made by the blood vessels. The cells were all of one type, but differed in size. They were polygonal in shape and contained chromaffine. A few giant cells with polymorphous nuclei occurred. Nerve elements could not be demonstrated. Associated with the tumor was marked hypertrophy of the left ventricle so that the heart weighed 500 grams, and since there was no other apparent cause for this, the author believes the hypertrophy to be due to chronic hyper-adrenalinemia.—D. J. G.

(ADRENAL) Spolia opima. Bland-Sutton (Sir J.), Brit. M. J. (Lond.), 1918, (ii), 593-597.

This paper, among other things, describes a malignant tumor of the adrenal in a man of 45. In 1912 the lower half of the humerus was excised, and found to be occupied by "a red and extremely vascular tumor presenting the naked-eye appearance of a myeloma." In 1918 the patient died suddenly, and post-mortem examination revealed the fact that both adrenals were converted into plum-colored masses as big as fists. The lower half of the right kidney, the abdominal lymph nodes and the heart were all involved in secondary metastases. The microscopic structure of the tumors in the adrenals and kidneys was found to be the same as that of the tumor in the humerus previously removed. Each consisted of an enormous number of thin-walled blood vessels, and resembled a cavernous naevus. The nodule in the heart had the same structure as the normal zona fasciculata of the adrenal gland. The remarkable feature of the case is its chronicity. It is pointed out that the pathological features presented by this case are similar to those that characterize the rare condition known as general thyroid malignancy in which a moderate, and apparently benign, enlargement of the thyroid gland is associated with multiple tumors, especially in the bones. The structure of such deposits is indistinguishable from that of normal thyroid tissue. The case presented is regarded as an example of "general adrenal malignancy."

—L. G. K.

ADRENAL reduction for the cure of epilepsy (Die Nebennierenreduktion als Krampfheilendes Mittel). Brüning. Deutsche med. Wchnschr. (Berlin), 1920, **46**, 1351-1353.

Technical details are given. Extirpation of an adrenal does not cure epilepsy, but is always followed by improvement and the irritability of the patients is much diminished after the operation. The patient must not be operated upon when he is too young, for then hypertrophy of the remaining adrenal may destroy the results. There exist also now and then accessory adrenals, which may influence the effect of the operation. The operation is only indicated in epilepsy with spasms. Petit-mal and epileptical somnolence are not improved by this treatment. In traumatic or Jackson's epilepsy it is necessary to remove first the primary cause in the brain. If this is not followed by improvement, reduction of the adrenal ought to be carried out.—J. K.

Treatment of spasms with extirpation of one of the ADRENALS (Zur Behandlung von Krämpfen mit Extirpation einer Nebenniere). Bumke (O.) & Kuttner (H.), Zentralbl. f. Chir. (Leipzig), 1920, **47**, 1410-1411.

Description of the technic of the operation.—J. K.

(ADRENALS) The cause of anaphylactic shock (Der Ursprung des anaphylaktischen Schockes). Forssman (J.), Biochem. Ztschr. (Berlin), 1920, **110**, 133-163.

Extirpation experiments on guinea pigs from which the adrenals were removed, and after recovery from the operation, into which acute lethal doses of sheep corpuscle hemolytic serum were intravenously injected, demonstrated that the resultant shock was neither weakened nor increased and that consequently adrenin cannot have a significant influence on its development.—F. S. H.

Changes in the chromaffin content of the ADRENALS in experimental diabetes of central origin (Über die Veränderungen des Gehaltes der Nebennieren an Chromaffiner Substanz bei einigen experimentellen Diabetesformen zentralen Ursprungs). Fujii (Ijuro), Tohoku J. Exp. Med. (Sendai), 1920, **1**, 38-72.

The methods of Negrin and Brücke, slightly modified, are used for estimating the amount of chromaffin material in rabbits killed by a blow on the head. In rabbits in which glycosuria developed following sugar puncture the chromaffin substance is decreased, but in those in which no glycosuria developed following sugar puncture there is no alteration. Eckhard's operation in three rabbits increases only very slightly the reducing substance in the medulla.

In four rabbits with splanchnics on one side cut, sugar puncture decreases the chromaffin substance on the side of the intact splanchnics. Sugar puncture in two rabbits with both splanchnics cut produces neither glycosuria nor diminution in chromaffin substance. Diuretic injection in six normal rabbits causes a temporary glycosuria and an increase in chromaffin, but diuretic injection in four animals with both splanchnics severed has no influence on glycosuria or adrenalin secretion.—E. V. C.

Similar processes of alterations, especially those of the ADRENALS (Fatti simili, descritti nella noto precedente in caso di alterazione principalmente delle capsule surrenali). Garibaldi (G.). Clin. dermosifilopat. d. r. Univ. di Roma, 1917, **35**, 61-68.

The author gives the history, characteristics, symptoms, and pigmentation disturbances of a case of acromegaly, in which hypertrophy of the adrenals is suspected. At autopsy the various organs were normal except the adrenals. These were enormously enlarged, firm in consistency, and reddish in color. Histological examination disclosed no difference between the pigment of the pathological areas and the main substance of normal organ. The entire mechanism of this hypertrophic alteration of the adrenals is considered as a vast phenomena of hemorrhagic infarction, produced by the pathological state of all the capillaries, the latter condition in turn being the result of weakness of the parenchymatous tissues. The author concludes by explaining that the phenomena, for processes that simulate tumors and the corresponding alteration of blood and vessels, is not a unique example of pathology. On the contrary, the condition can be verified by any case of leucocytosis or of syphilis. —D. P.

Relation between splanchnic nerve function and ADRENAL secretion. Gley (E.) & Quinquaud (A.), Acad. r. Belg. bull. cl. d. sc., No. 4, pp. 315-316.

The authors supplement the report of researches published in 1914 and arrive at the conclusion that there is no such thing as physiological epinephrinemia. (See previous abstracts in Endocrinology.) Physiol. Abst., **5**, 40.

(ADRENAL) Gastric superacidity. Hayes (W. V.), N. York M. J., 1920, **112**, 5-8.

Hyperacidity may result because of nervous disorders, mental states, and reflexes from parts of irritation, especially of the gastrointestinal tract. Gastric secretions may also be excited by the stimulating action of foods and hormones. Certain cases of hyperacidity are readily controlled and benefitted by the administration of adrenal nucleoproteid and adrenal extracts.—H. W.

(ADRENALS) Hypertension and arterial fibrosis. Hood (C. T.), N. York M. J., 1920, **112**, 152-156.

An increased salt concentration in the tissues results in an accumulation of fluid therein and an increased capillary tension which requires in turn an increased systolic pressure. This condition demands an extra effort on the part of the left ventricle which may in time result in hypertrophy of the left ventricle or of the entire heart. In **Addison's disease** there is a low salt concentration, hence, on the basis of the above statements, such low pressures are to be ascribed to the lack of a sufficiently high salt concentration in the body tissues.—H. W.

(ADRENAL) Changes in organ weight produced by diets deficient in antiscorbutic vitamine. LaMer (V. K.) & Campbell (H. L.), Proc. Soc. Biol. & Med. (N. Y.), 1920, **18**, 32.

Young guinea-pigs weighing 250-300 grams, fed on a diet deficient in water-soluble C (antiscorbutic vitamine), show at death a pronounced increase in weight of the adrenal glands amounting to approximately 100 per cent. when computed on basis of body weight minus alimentary canal. (Confirming McCarrison's statement.)

The increase in size is equally definite but not so pronounced when computed on basis of the beginning, or maximum, body weight attained. Starvation controls do not show an increase in adrenal weight.

The increase in adrenal weight is directly proportional to the length of time which the animal is on the scorbutic diet and is most pronounced in those animals in which life has been prolonged by affording them partial protection with small but insufficient quantities of tomato juice.

This may be interpreted as indicating a compensatory response to the decreased adrenalin production known to exist in the scorbutic animal. This point is of interest in connection with the extensive intramuscular and intestinal hemorrhages found in scurvy. —Quoted.

ADRENALS, enlargement of the—in a fatal case of DIABETES. Litchfield (W. F.) & Little (E. M.), Med. J. Australia (Sidney), 1917, **2**, 73-74.

A post-mortem report of a case of diabetes in a woman of 53 terminating fatally in coma some time after two operations from gangrene of the extremities. The **spleen** was small and hard. The **pancreas** was atrophied and hard. The adrenals were both much enlarged. The **hypophysis** appeared to be normal. Microscopically the pancreas showed a fine fibrosis and the islands of Langerhans were present in normal numbers. The adenal cortex was increased.

The authors consider that some agency produced an adrenal hyperfunction and hypertrophy, which in turn induced the diabetes and ultimately caused the pancreatic fibrosis.—F. S. H.

ADRENAL preparations and their activity on peroral administration (Versuche über die Wirksamkeit der Nebennierenpräparate bei peroraler Zufuhr.) Loewe (S.) & Simon (Marie), Ztschr. f. d. ges. Exp. Med. (Berlin), 1918, **6**, 327-334.

Using rabbits, the authors carried out a series of 23 experiments in which they studied the absorption of adrenin administered by mouth by its effect on the peripheral vessel. It was found that an active preparation failed to produce any significant narrowing of the vessels or antiphlogistic action as is observed to a marked degree when the substance is injected subcutaneously or intravenously. Consequently, massive doses must be given **per os** for effectiveness.—F. S. H.

(ADRENALS) Addison's disease (Beitrag zur Kentniss der Addisonschen Krankheit). Löffler (W.), Zeitschr. f. klin. Med. (Berlin), 1920, **90**, 265-285.

Five cases are reported. Post-mortem examinations were made on four of them with the following pathological findings: The medulla of the **adrenals** was completely changed into tuberculous caseous tissue; the cortex was largely destroyed by tuberculous granulations; in all cases normal tissue could be found in the cortex, showing signs of regeneration. It is probable that first the medulla had become affected and the cortex had been secondarily attacked. In none of these cases were cells found either in the plexas solaris or the "Grenzshang" of the sympathetic that were chrom-staining. In a fifth case with tuberculous changes in the lungs, the liver, **spleen,** kidneys, **prostate,** adrenals and peritoneum. Both adrenals contained much normal cortical and medullary tissue. Status lymphaticus or **thymolymphaticus** was found in two of the five cases. In two others there were only a few symptoms of status lymphaticus; in the fifth case no signs of a status could be detected.—J. K.

ADRENAL paraganglioma (Le paragangliome surrénal). Peyron (A.), Ann. de l'Inst. Pasteur (Paris), 1917, **31**, 313-367.

Two types of epithelial tumors are recognized as springing from the suprarenal capsule; that arising from the chromaffin tissue of the medulla is known as "paraganglioma," while the tumor originating in the cortex is called "cortico-suprarenaloma." Mixed types involving both cortex and medulla are not believed to occur. Paragangliomata are of far less frequent occurrence than are the cortical tumors, and are rarely malignant, the author describing the

first known case. Most of the work was done on tumors found in the horse, but one case of a paraganglioma in a sheep is also recorded. Histologically, the primary paraganglioma in the horse takes the form of gland-like epithelial cavities, often of considerable size and of variable form. These represent the axial cavities of the normal suprarenal in an enlarged and altered form. Another important characteristic is the presence of cellular masses or strands of dense cytoplasm with small nuclei, resembling the chromophobe cells of the **hypophysis.** These nests of multi-nuclear cells represent a form of cellular renewal and multiplication. Intravacuolar secretion of chromaffin granules occurs, accompanied by the disappearance of the nuclei of many of the cells. Whether an adrenalaemia occurs or not is left for others to settle. The histology of the one case of malignant paraganglioma on record is also fully described. The metastases seem to spread largely by the venous system. In this case they were found in the kidney, lungs and a lumbar ganglion.—L. G. K.

(ADRENAL) Suprarenal sarcoma of the Robert Hutchison type. Weber (F. P.), Brit. J. Child. Dis. (London), 1920, **17,** 133-139.

Weber reports a case of what was evidently primary malignant disease of the medullary portion of the right suprarenal gland with multiple secondary metastases in the cranium of the type collected by Robert Hutchison. The patient was a girl of five years of age with a family history which was negative in every respect. Her liver was enormously enlarged, occupying most of the front of the abdomen and palpable as far down as the pelvis on the right side. The **spleen** was not felt. The eyes were both swollen and ecchymotic. The child was nearly blind in both eyes for almost a month. Opthalmic examination showed both optic discs to be pale with blurred edges, indicating a condition of post-neuritic atrophy of the optic nerve; there were no retinal hemorrhages. Because of this involvement of the skull and orbits and the presence in some cases of decided exophthalmos, Weber states that the cases may at first sight be regarded as chloroma or some form of acute or subacute leukemia, but this error could be avoided in the majority of instances by a careful examination of the blood.

The child died. Autopsy showed a tumor the size of a big orange, but of irregular shape, attached to the upper pole of the right kidney. It showed actively growing nodules which microscopically had the appearance of round cell sarcomas. It doubtless originated in the medullary portion of the right suprarenal gland and remains of suprerenal cortical tissue could be made out by microscopical examination in the layer of compressed capsule-like tissue enclosing the neoplasm. Weber, however, changed his original diagnosis of sarcomatous origin after reading Douglas Symmer's

paper on "Recurrent neuroblastoma" and came to the conclusion that the tumor in the right suprarenal in his case was, like others of this type, really a malignant hypernephroma of the suprarenal medulla, not of sarcomatous origin but of neuroblastomatous nature. The liver showed tumor cells resembling those found in the suprarenal. The kidney, left suprarenal and spleen were normal. There were metastatic growths in the abdominal lymph glands, cranial cavity, orbits, ovaries and dura mater, all resembling the suprarenal neoplasm. There were no growths in the brain itself. Perhaps the two most valuable diagnostic signs, according to Weber, of the Robert Hutchison type during life are: first, the dark ecchymotic swellings of the eyelids on one or both sides with or without exophthalmos, and, secondly, the optic neuritis or post neuritic atrophy. In the absence of both of these signs, one ought to hesitate in regard to the diagnosis.—M. B. G.

(ADRENAL) Observations in connection with the early development of the human suprarenal gland. Wieman (H.), Anat. Rec. (Phila.), 1920, **19**, 269-279.

An embryological study based on one 9 mm. and one 12 mm. human embryo.—W. J. A.

(ADRENALS) The Diagnosis of Suprarenal Tumors, especially in regard to Blood Pressure. Weber (F. P.), Practitioner (Lond.), 1920, **105**, 181-185.

A very brief, sketchy article, but calling attention to some interesting clinical aspects. Suprarenal tumors metastasize, as do malignant thyroid neoplasms, especially in the bones. Mention is made of the "infant hercules type," the precocious child resulting from primary tumors of the suprarenal cortex. Attention is called to the "Robert Hutchinson type" of malignant suprarenal tumors in children with metastases in the cranium, frequently so located as to produce a characteristic proptosis with ecchymotic edema of the eyelids. Scurvy with intraorbital hemorrhage, and chloroma can be readily differentiated. The blood pressure in these cases, even in children, is apt to be raised.—H. L.

ADRENIN, and vitamine in the treatment of the otosclerotic syndrome (L'adrenalina et le vitamine nel trattamento della sindrome otospongiosica [otosclerosi]). Caldera (C.), Arch. ital. d. otol (Napoli), 1920, **31**, 11-15.

The author obtained very good results when giving adrenin orally in cases of otospongiosis both as regards improvement in taste and improvement in hearing. Since the disorder has a patho-

logical-anatomical analogy to rachitis the author also fed vitamines with equally good results, though unfortunately the period of observation is as yet too short to allow definite conclusions to be drawn. From: Ber. d. ges. Physiol. u. exp. Pharm. (Berlin), 1920, 3, 340.
—F. S. H.

Antagonism of depressor action of small doses of ADRENALIN by tissue extracts. Collip (J. B.), Am. J. Physiol. (Balt.), 1920, **53**, 477-482.

The fall in blood pressure following small doses of adrenalin is antagonized by various tissue extracts, while the rise in pressure produced by larger doses is augmented and prolonged. Both effects are of the same order.—T. C. B.

Antagonism of inhibitory action of ADRENALIN and depression of cardiac vagus by a constituent of certain tissue extracts. Collip (J. B.), Am. J. Physiol. (Balt.), 1920, **53**, 343-354.

Of endocrine interest is the fact that "extract" of heart, **spleen, pancreas, testes, anterior and posterior lobe of the pituitary thymus, thyroid** and **parathyroid** glands, in addition to stimulating the uterus of the rat, guinea pig, virgin dog and cat, antagonized the inhibitory action of adrenalin on these organs. Intravenous injections of extract of spleen augments the pressor response to adrenalin.
—T. C. B.

Effect of ADRENALIN on venous blood pressure. Connet (Helene), Am. J. Physiol. (Balt.), 1920, **54**, 96-121.

The venous pressure rises in dogs and cats after intravenous injections of adrenalin. The two factors chiefly responsible are the decreased heart rate diminishing the unit output, and a vaso-constrictor mechanism in the veins. In anesthetized dogs with good vagal tone the rise is due to the first factor. In cats the second factor predominates.—T. C. B.

Adrenalin in the Treatment of Vertigo (L'adrenalina nella cura delle vertigini). D'Arbela, Riv. Crit. di Clin. Med., (Firenze), 1920, **21**, 250-251.

Starting from the statement that vertigo is the subjective expression of a sympathetic vaso-tonic unbalance of the Labyrinth, made by Vernet in the Presse Med. of July, 1920, adrenalin should be the ideal treatment. Adrenalin is supposed to excite the sympathetic nervous ends, to regulate the blood pressure and to be antitoxic. Therefore it has been employed with result at the dose of five drops to twenty drops twice a day. The A. treated these last four years numbers of patients suffering from vertigo with very encouraging results.—G. V.

Diminished renal permeability for sugar in experimental ADRENIN diabetes (Die sogenannte Nierendichtung gegen Zucker beim experimentellen Adrenalin diabetes). Hildebrandt, Deutsche med. Wchnschr. (Berlin), 1920, **46**, 1436.

Pollack has stated that when adrenin is injected regularly into animals the kidneys lose their permeability for sugar and that therefore the injection on the second or third day no longer gives rise to glycosuria. Hildebrandt has determined the blood sugar content by Bang's micro method and cannot confirm this. The reason why no glycosuria is observed is not a loss of permeability of the kidney but simply that repeated injections often do not cause hyperglycemia. The work of Pollack is worthless as he worked with the Bertrand method, where it is necessary to tie the animal; the method of getting the blood is painful and much blood is wanted. We know, however, that all these facts (loss of much blood, tying of the animal, pain) have an important influence on the blood sugar.—J. K.

ADRENIN mydriasis in chronic nephritis (Die Adrenalin mydriasis bei Chronischer Nephritis). Kato (Toyojiro) & Watanabe (Masao), Tohoku, J. Exp. Med. (Sendai), 1920, **1**, 187-191.

A critical review of the literature on adrenin mydriasis with observations showing that this reaction becomes more marked in chronic nephritis with increase in blood pressure.—E. V. C.

ADRENIN injections as a method of treatment of hemorrhoids (Ueber die Behandlung der Hämorrhoiden mit Suprarenininjektionen). Krukenberg (H.), München. med. Wchnschr., 1918, **65**, 851-852.

The parenchymatous injection of 1:1000 adrenin in cases of hemorrhoids causes a rapid diminution of the disturbance. The single administration of a 0.5 cc. dose caused the complete disappearance of the swellings in the course of eight days.—F. S. H.

ADRENIN, Treatment of the vomiting of pregnancy (Les vomissements incoercibles de la grossesse et leur traitement par l' adrenaline). Rathery (F.) & Bordet (F.), Ann. méd. (Paris), 1920, **8**, 94-100.

The authors obtained success in the treatment of the pernicious vomiting of pregnancy by the use of adrenin. They prescribed the subcutaneous injection of one-half milligram of adrenin chlorhydrate in 250 cc. of normal saline solution, and the ingestion or rectal administration of one-half milligram of the same preparation the first day with the dose to be doubled by both methods of administration on the next two or three days, and then cut down to the original dose, depending on the results obtained. The pa-

tients usually responded well within 24 to 48 hours. Whether or not the pernicious vomiting is due to an adrenal insufficiency is a question, but in the cases presented the administration of adrenin did not have any influence whatsoever on the arterial tension.

—F. S. H.

(ADRENIN) Reactions following intravenous administration of arsphenamine. The influence of atropine sulphate and adrenalin chloride upon these reactions. Strickler (A. A.), N. York M. J., 1920, **112**, 498-499.

The injection of 0.5 cc. of adrenin or 1/75 grain atropine previous to arsphenamine injections in no way influences the occurrence of reactive phenomena.—H. W.

A clinical apparatus for measuring BASAL METABOLISM. Benedict (F. G.) & Collins (W. E.), Boston M. & S. J., 1920, **183**, 449-458.

A comparison of the results of basal metabolism determinations obtained using a simplified apparatus with those obtained with the older and more complicated types of apparatus. The results of the simplified method are as accurate and more easily obtained than those by the older methods.—H. W.

(CARBOHYDRATE METABOLISM) On the metabolism of glucose in surviving organs (Sur le métabolisme de la glycose dans les organes survivantes). Lombroso (U.) & Artom (C.), Arch. ital. de biol. (Pise), 1917, **67**, 244-272.

Data published elsewhere. See Endocrinology, 1919, **3**, 190.

—L. G. K.

(CARBOHYDRATE METABOLISM) On the metabolism of glucose in surviving organs (Sur le métabolisme de la glycose dans les organes survivantes). Lombroso (U.) & Luchetti (C.), Arch. ital. de biol. (Pise), 1918, **68**, 145-147.

Not of endocrine interest.—L. G. K.

Further observations on the functions of the CORPUS LUTEUM. Ochsner (E. H.), Surg., Gynec. & Obst. (Chicago), 1920, **31**, 496-501.

The author quotes the experience of veterinarians to show that the retention of a false corpus luteum in the cow prevents the onset of the period of heat. If this corpus luteum is manually expressed the cow invariably comes in heat within 48 to 120 hours. Similarly the rupture or excision of a false corpus luteum in woman brings on menstruation within 12 to 36 hours. A number of cases are cited in support of this view. The following conclusions are

then drawn: (1) That an unabsorbed false corpus luteum prevents ovulation and is a common cause of sterility, and that the expression or excision of such a false corpus luteum invariably brings on menstruation. (2) That the excision or rupture of a true corpus luteum invariably results in interruption of pregnancy at least during the early months of pregnancy, and that it may be looked upon as a common cause of abortion. (3) That an injury to either the true or false corpus luteum may simulate ruptured extrauterine pregnancy.—L. G. K.

The role of fat in DIABETES. Allen (F. M.), Harvey Lect. (Phila. & Lond.), 1916-17, Series **12**, 42-111.

Data published elsewhere. Contains an extensive bibliography on the subject. See Endočrinology, 1919, **3**, 365 and 554.—L. G. K.

(DIABETES) Healing of a trophic ulcer of the great toe in an aged glycosuric patient. Barlow (H. C.), Brit. M. J. (Lond)., 1920, (ii), 124-125.

The patient was 82 years of age and had suffered from diabetes for twenty years. The ulcer healed completely after about five months of thorough local treatment and a reduced carbohydrate and fat intake. Sugar was still present in the urine however.—L. G. K.

(DIABETES) The relation of the islets of Langerhans to diabetes with special reference to cases of pancreatic lithiasis. Barron (M.), Surg., Gynec. & Obst. (Chicago), 1920, **31**, 437-448.

Pancreatic lithiasis is a very rare disease, which occurs mostly in males during the fourth decade. The obstruction of the pancreatic duct leads to an advaced atrophy of the pancreas accompanied by more or less fibrosis. The islets may remain intact even when the acini disappear completely. The islets are epithelial structures which are entirely independent of the acini and have no relation or communication with the ducts. Changes in the islets —such as degeneration, necrosis and fibrosis—generally occur late in the disease, probably as a result of a superimposed secondary infection, consequent to a prolonged stasis in the ducts. In complete accord with the results of animal experimentation occlusion of the ducts by calculi in man does not result in diabetes mellitus unless there be actual injury to the islets. Cases of pancreatic lithiasis presenting symptoms of hyperglycaemia and glycosuria reveal definite lesions of the islets at autopsy. The author's study thus bears out the conclusions that the islets secrete a hormone directly into the lymph or blood streams, which has a controlling power over carbohydrate metabolism. The histopathology of the islets in diabetes falls into three main types, which in order of their importance, are as follows: fibrosis, hyaline degenration, and

arteriosclerotic changes. The pathogenesis of these lesions may not be very dissimilar to that of nephritis when taken in the broad sense. The difference in intensity of the pathological changes in the kidney as compared with those in the pancreas may be explained by the marked difference in the character of the two organs. In the kidneys any glomerulitis or other changes in the glomeruli are followed or accompanied by alterations in the tubules; no such changes affect the tubules or acini in the pancreas, since the islets are entirely distinct from the latter structures.—L. G. K.

DIABETES in relation to the DUCTLESS GLANDS. Brown (W. L.), Brit. M. J. (Lond.), 1920, (ii), 191-194.

The author classifies glycosuria as (1) organic in origin, with structural changes in the endocrine glands leading to (a) overaction of the **thyroid, adrenal, pituitary** or (b) underaction of the **pancreas**; (2) sympathetic in origin, with no evidence of structural changes in any endocrine gland, but producing a functional (a) overaction of the adrenal, thyroid, pituitary, and (b) underaction of the pancreas. Ordinary diabetes shows no other signs of endocrine disease, while endocrine glycosuria betrays other evidences of that origin. The most reliable signs of organic disease of the pancreas are (1) an excess of unsplit fat in the stools; (2) a high diastase content in the urine; (3) the adrenalin eye test. Jaundice would further suggest that the head of the pancreas was involved. Graves' disease and pituitary affections are frequently associated with glycosuria but the case for a definite adrenal diabetes is not clear. Diabetes is, then, a sign of exaggerated metabolism evoked through the sympathetic and the associated endocrine glands, which first asserts itself in relation to the most abundant food material (carbohydrate), but as it advances expresses itself in relation to all. The treatment by alimentary rest is advocated, the effect of which is to slow down metabolism and to increase the production of pancreatic internal secretion by diverting the pancreatic activity from the production of external secretion.—L. G. K.

DIABETES et syphilis. Bouchard (J.). Thése de Lyon. 1920.

The author comes to following conclusions:

There exist cases of glycosuria and diabetes that begin after a syphilitic infection. This may happen in the secondary or tertiary stages. Often the symptoms of secondary or tertiary syphilis begin at the same time as the diabetes. There are cases of diabetes which are markedly improved or even cured by antisyphilitical therapy. Syphilis acts as a malignant growth and may produce diabetes by local changes in the brain or in the liver and pancreas. On the other hand, it is possible that syphilis acts on the whole organism and produces diabetes by "humoral disturbances." When

there are symptoms of syphilis in a patient with diabetes it is necessary to begin antisyphilitical treatment.—J. K.

DIABETES and pancreatic insufficiency: treatment by opotherapy: therapeutic differentiation of the external and the internal secretions of the pancreas (Diabète avec insuffisance pancréatique: traitement opothérapique: disjonction thérapeutique des sécrétions externe et interne du pancréas). Faroy (G.), Bull. et mem. Soc. méd. de hop. de Par., 1919 **43**, 234-237.

Corrected citation; see Endocrinology, **4**, 146.—F. S. H.

Treatment of DIABETES (Zur Therapie der Diabetes). Grafe. München. med. Wchnschr., 1920, **67**, 1453.

The data have been reported in an abstract from Deutsch. Arch. f. klin. Med.—J. K.

DIABETES, mortality in the different branches of trade in adult men in Danish towns. Heiberg (K. A.), Ugesk. f. Laeger (Copenhagen), 1916, **78**, 174-179.

The author has collected from the public health archives the cases of deaths from diabetes in the period 1904-14. He found the mortality rate was 2%. There was no apparent difference between the mortality in the different social classes (intellectual workers, farmers, tradesmen, etc.).—K. H. K.

DIABETES, Relation of the alkali reserve of the blood to glycosuria and hyperglycemia in pancreatic—. Hendrix (Byron M.) & Crouter (Caroline Y.), J. Biol. Chem. (Balt.), 1920, **45**, 51-55.

The authors of this report started with the idea that if the gastric juice were not completely neutralized in the intestine after the removal of the pancreas, it would react with the carbonates and phosphates of the blood in the portal system causing a reduction of the alkali reserve in the whole blood, inasmuch as the blood from the portal system is mixed with the blood from the rest of the body in the heart, lungs and to a less extent, in the liver. Since hyperglyceria and glucosuria appear very soon after the removal of the pancreas, it was thought worth while to study the alkali reserve of the blood as measured by the power of the plasma to combine with carbon dioxide, and compare this with the change in the concentration of glucose in the blood, and its excretion into the urine.

Five dogs were used in the study, two males and three females, one of which was pregnant. It was found that the alkali reserve of the blood as measured by the carbon dioxide of the plasma showed no increase until diabetes, as shown by the G:N ratio and increase in blood sugar, had been established for at least 24 hours. The earliest appearance of a decrease in the carbon dioxide ca-

pacity of the blood came about 48 hours after the removal of the pancreas, while there was always a definite increase in the blood sugar within one day after the operation. It is well known that glucose appears in the urine a few hours after removal of the pancreas.—F. S. H.

(DIABETES) Pre-operative preparation of diabetic patients and their subsequent treatment. Kahn (M.), Surg., Gynec. & Obst. (Chicago), 1920, **31**, 363-365.

The patient's degree of acidosis should be determined, and then corrected by reducing the fat intake to a minimum and by stimulating the carbohydrate oxidation, because of its anti-ketogenic powers. The diet therefore should be poor in fat and rich in vegetables and proteins, with the addition of a cereal which adds to the carbohydrate content. Sometimes alcohol may also be used to advantage. Alkalies should not be prescribed. The bowels should be kept open, preferably by enemata, in order to avoid draining the alkali salts from the body. Fluids should be administered in liberal amounts. Finally by the plan of Allen or by a modified starvation diet the glucaemia may be reduced. Nitrous oxide is the anesthetic of choice. In the after-treatment the glucose tolerance should be constantly increased. Caffeine is contra-indicated as a stimulant. Large doses of calcium chloride are advised, 10 gr. three times a day after meals.—L. G. K.

Yoghurt treatment of DIABETES (Yoghurtkuren bei diabetes). Klemperer (G.), Berl. klin. Wchnschr., 1918, **55**, 523-524.

The author describes the results obtained by treating six cases of diabetes with the daily addition to the diet of one liter of yoghurt milk. As a result of the ingestion of this substance the glucosuria disappeared or was markedly reduced. Notice is also made of the fact that eight other diabetics of more or less intensity showed an increased sugar output under the treatment instead of a diminution. Klemperer is of the opinion that the beneficial effects were due to the Yoghurt bacilli and that the deleterious action was due to the overwhelming of these by other intestinal bacterial forms.—F. S. H.

Fruit days in DIABETES mellitus (Früchtetage bei Diabetes mellitus). Lampé (E.), Therap. Monatshm. (Berl.), 1918, **32**, 337-338.

A brief article advocating the inclusion of a fruit day in the dietary regime of diabetics.—F. S. H.

DIABETES mellitus, particularly war diabetes, treated with enzymes (Zur Fermentbehandlung des Diabetes mellitus, speziell des Kriegsdiabetes). Lennè. Deutsche med. Wchnschr. (Berl. u. Leipz.), 1918, **44**, 39-40.

Lennè reports the effects of a commercial enzyme preparation "Diabetylin" in five cases of diabetes mellitus. The originators of the product state that it is a combination of trypsin with yeast, which "promotes glycolysis." The feeding of the product failed to cause any decrease in the glucosuria or amelioration of the patients.—F. S. H.

DIABETES accompanied by generalized xanthomatosis. (Generalizerte Xanthomatose bei Diabetes). Lubarsch (O.), Deutsche med. Wchnschr. (Berl. u. Leipz.), 1918, **44**, 484-486.

Data reported elsewhere.—F. S. H.

The treatment of DIABETES MELLITUS. Mason (E. H.), Canad. M. Ass. J. (Toronto), 1920, **10**, 1105-1111.

The following is an outline of the method used in treating diabetic patients in the Royal Victoria Hospital, Montreal: (1) Obsevation diet (for 3 days) containing—protein, 1.5 gm. per kilo body weight; fat, enough to make 20 or 25 calories per kilo; carbohydate, 1 gm. per kilo. (2) One-half observation diet. (3) One-quarter observation diet. (4) Fast. This period includes thrice boiled vegetables, bran cakes and chicken broth. (5) Determination of carbohydrate tolerance upon green vegetables increasing 10 gm. of carbohydrate per day until there is glycosuria 2 days in succession on the same intake of carbohydrate. (6) Fast, to free from glycosuria. (7) One-third trial maintenance diet. (8) Two-thirds trial maintenance diet. (9) Trial maintenance diet containing, protein, 1.5 gm. per kilo body weight; fat, enough to make 25 calories per kilo; carbohydrate, half that of the carbohydrate tolerance as detemined on green vegetables. (10) Increases above the trial maintenance diet depends upon the case, it often being wise to give 1.75 gm. of protein per kilo, a slightly larger amount of carbohydrate, or fat enough to make 30 to 35 calories per kilo body weight. After the determination of the carbohydrate tolerance upon green vegetables a regular weekly fast or one-half value day is instituted. This is continued after discharge, for it is believed to be an important factor in the ultimate improvement of the case. During the patient's stay in the hospital he is carefully educated in the nature of his condition, normal metabolism, the technique of figuring diets, kitchen work, and laboratory methods for detecting glucose and acetone in urine. On discharge he is furnished with the means of carrying out his instructions. It is found that the results vary directly with the thoroughness of the patient's education while in the hospital, and the carefulness with which their diets are supervised after their discharge.—L. G. K.

DIABETES, The diet in— (Le regime alimentaire des diabetiques). Nigay, J. de méd. de Paris, 1917, **36**, 172-174, 189-191, 209-212, 229-231; 1918, **37**, 8-10: 28-29, 50-52, 72-73, 95-96, 110-111, 130-131.

Nigay recommends fatty soups, and cabbage soup by virtue of its alkaline salt content. Hors d'oeuvres are allowable because of their high fat content. Milk is prohibited unless previously desaccharated in the form of kéfir, koumyss, etc. Eggs are looked on with favor. Fish in general is acceptable because of the high fat and protein content. Salt fish, however, is in disfavor. All meats save that from the horse can be eaten readily but within reason. Diabetics possessing a good digestive tube can eat fats in all their forms without limit. Vegetables are advocated as a good source of filling material, fresh peas, beans, lentils, etc., are permitted. Potatoes are forbidden fruit. Non-farinaceous gravies are allowable but condiments are frowned upon, as is pastry. Cheese is persona grata. Bread and cake, unless prepared by special formulae, are taboo. Dry wines and other alcoholic beverages, coffee, tea (mint and camomile) and mineral waters are permitted. The articles continue with descriptions of when the diabetics should eat, the proper diet for irreducible glycosuria, for diabetes complicated by dyspepsia, eczema, prurigo, gout, albuminuria, uremic nephritis, acidosis and inanition, on the diet sufficient to prevent denutrition.—F. S. H.

DIABETES MELLITUS and the war (Kreigserfahrungen über Diabetes mellitus). Richter (P. F.), Deutsche med. Wchnschr. (Berlin), 1920, **46**, 1380.

During the war the mortality in Germany from diabetes was greatly diminished, even up to 100%. In England, where there was much more food, though less than before the war, the mortality diminished 25%. Perhaps many patients with diabetes died from tuberculosis. The cases of severe acidosis have nearly disappeared; in its place cachexia has become much more frequent. The light cases have much improved. Many show a glucosuria, though nearly always hyperglycemia. It is of great importance to restrict the diet in regard to proteins. This is more important than underfeeding.—J. K.

A case of transitory hypermetropia in DIABETES. Rönne (H.), Hosp.-tid. (Copenhagen), 1916, **59**, 195-196.

A woman aged 46 years showed subjective signs of diabetes for a month; there was 8% glucose in the urine. One morning she suddenly could not see distinctly. The eye examination showed sight 6/6, hypermetropia 3.00 diopters. After a month she could not see through her glasses of 3.00 diopters, but the sight was good without these. A new examination showed sight 6/6, and hyper-

metropia 0.50 diopters. Such cases, but less acute, have been described before. The changes are probably related to changes of tension in the lenticular fibres caused by chemical reaction. In the discussion Lundsgaard remarked that most cases of hypermetropia in diabetes are not detected. It is uncertain if the changes of glucosuria cause the disease. Ask has found a certain proportion between the content of glucose in the aqueous humor and the blood-plasma.—K. H. K.

The prevention of DIABETES MELLITUS. Williamson (R. T.), Practitioner (Lond.), 1920, **105**, 233-243.

Diabetes is more apt to develop where there is a family history of the disease, in those whose brains are greatly overworked, in those who take too much sugar, sweet foods, or drinks, in those who take too little exercise, and those who are very stout, and eat too much. Diabetes is more prevalent in Maltese, Hebrews, Hindus and in the citizens of the United States. Excess of starchy carbohydrate food probably does not increase the risk of diabetes; diabetes, for instance, is not especially prevalent among Chinese. Sugar is more injurious than starch. Williamson recommends as preventive measures: 1 Avoid great excess of sugar, jam, sweets, chocolate, sweet foods, sweet drinks; 2 If there be positive family history or race tendency, no sugar should be added to any food or drink; a list is given of very sweet foods, fruits and drinks which should be avoided; 3 Obesity should be checked; 4 Sufficient physical exercise is important; 5 Excessive brain work and nervous strain should be avoided; 6 Restriction of alcoholic drinks; 7 Sufficient sleep; 8 Conservative diets should be recommended in diseases in which diabetes is not an infrequent complication such as **Graves' disease, acromegaly,** chronic gout, chronic Bright's disease and arteriosclerosis.—H. L.

The decreased resistance of patients with DIABETES towards infections (Über die verminderte Resistenz Zuckerkranker gegenüber pyogenen Infektionen). Wolfsohn (G.), Ztschr. f. ärtzl. Fortbild. (Jena), 1920, **17**, 678-679.

The phagocytic properties of the leucocytes of diabetic patients are less marked than are those leucocytes from normal individuals.
—J. K.

DIABETIC XANTHOMA, demonstration of preparations (Demonstration anatomischer Präparate von Xanthoma diabeticum). Lubarsch (O.), Berl. klin. Wchnschr., 1918, **55**, 196.

Macroscopic and microscopic preparations from a young diabetic showed a generalized xanthomatosis. The pigmentation was particularly marked in the liver, spleen and lymph-nodes.—F. S. H.

Influence of the DUCTLESS GLANDS upon amphibian metamorphosis. Hogben (L. T.), Science Prog. (Lond.), 1920, **15**, 302-306.

An essay dealing with the more recent work on amphibian metamorphosis as influenced by the various endocrine glands.
—T. C. B.

On some ENDOCRINE GLANDS (Die alcune ghiandole endocrine). Anon. Morgagni (Milano), 1920, **62**, 513-518.

A general superficial review.—J. K.

(ENDOCRINE GLANDS) Endocrinopathic nanism accompanied by multiple dystrophies (osseous and visceral); Raynaud's syndrome and dementia precox in a case of hereditary syphilis (Nanismo endocrinopatico, coincidiendo con multiples distrofias [oseas y viscerales], Syndrome de Raynaud y demencia precoz, en una sifilitica hereditaria adulta). Castex (M. R.) & Waldorp (C. P.), Rev. Asoc. med. argent. (Buenos Aires), 1920, **32**, 270-273.

Report of a patient 25 years old, 1.30 m. tall and weighing 25 kgr. Anatomical examination of the hypophysis and adrenals showed them to be normal. There was genital hypotrophy and mild thyroid sclerosis. The lesions are attributed to hereditary syphilis.
—B. A. H.

(ENDOCRINE GLANDS) Diffuse Neurofibromatosis (Recklinghausen's Disease) (Neurofibromatosi diffusa [Morbo di Recklinghausen]). Castronuovo (G.), Riferma Med. (Napoli), 1920, **36**, 817-821.

The author gives a detailed description of the disease, reporting a case, which showed a precocious association of tuberculosis, whose asthenic conditions improved for a time with administration of large doses of **adrenin**. In the pathogenesis he lays a great stress on the endocrine disturbances—pluriglandular, but especially connected with adrenal, **hypophysis, ovary** and **thyroid** dysfunction —and, following Castellino's opinion, relates neurofibromatosis to acromegaly, Addison's disease and Dercum's disease, which all show, besides cutaneous and subcutaneous alterations, characteristic disturbances of the blood and of the metabolism. Their relationship is furthermore demonstrated by their frequent association, by their passing from one to another and finally by the improvement shown in them all with hormonic therapy (adrenal, hypophyseal, thyroid).
—G. V.

ENDOCRINOLOGY, general physiology and the thyro-parathyroid system. Delgado (H. F.), Crón. Méd. (Lima), 1920, **37**, 281-292.

A critical review containing no new data.—I. O.

(ENDOCRINE GLANDS) Sterility, sex stimulation and the endocrines. Edgar (T. W.), N. York M. J., 1920, **112**, 848-849.

From a limited number of observations following the administration of Edgar's pluriglandular serum, the author concludes that certain cases of sterility and sex depletion are, like **diabetes**, the result of endocrine want. Old age may also be placed in the category of endocrine want. It is possible that the pluriglandular serum of which so much has been claimed by Edgar, does relieve a great number of diabetics. However, the claim that the same serum reinstates sexual life may be explained by the fact that any general building up of the body results in an increased libido and sex life.
—H. W.

The ENDOCRINES in gynecology. Graves (W. P.), N. York M. J., 1920, **112**, 697-701.

The author considers that functional neuroses are continuous states of emotional excitement which are sensory in character induced by reciprocal activities following stimulation of the autonomic nervous system and certain of the glands of internal secretion.
—H. W.

(ENDOCRINE GLANDS) Infantilisme. Krabbé (K. H.), Nord. med. Ark. (Stockholm), 1919, **51**, 551-578.

The author describes 4 cases of infantilism in adults, a case of arrested development, without arrest of sexual development, and two cases of arrested development in children, which possibly may show infantilism after puberty. One of the cases was connected with Calvé-Perthes disease, another one with epilepsy. The three cases did not show any sign of endocrinal disease apart from infantilism. The author concludes that the basis of infantilism is a combination of arrest of sexual development with general arrested development, and not so much the psychic relations or the infantile proportions which in many cases may be modificated by several complications. As shown before, infantilism may be produced by **thyroid** or **hypophyseal insufficiency** (but not by **ovarian** or **testicular**). Besides these cases of dysendocrine infantilism many cases exist of infantilism in which no signs of endocrinal disease may be shown. Perhaps some of these cases are dysendocrine, but it is still not proved and we must temporarily acknowledge our ignorance concerning the pathogenesis of these cases. (The article is in French.)—K. H. K.

(ENDOCRINE GLANDS) Two cases of Apert's hirsutism, virilism and psychopathy (Deux cas d'hirsutism d'Apert avec virilisme et psychopathie). Laignel-Lavastine & Boutet (A.), Bull. et mém. Soc. méd. d. hôp. Par. 1920, **44**, 1303-1313.

A report of two female patients. The first presented general hypertrichosis and confusional anxiety which apparently was aligned with Basedow's syndrome, ammenorrhea and mitral regurgitation. There was mental debility, melancholy depression, mutism, etc. A hyperchloresterinemia was present, which when correlated with the arterial hypertension, a facile glucosuria and reaction to the glandular tests led to the diagnosis of a **hyperadrenalemia** probably as a reaction from **ovarian** insufficiency. The endocrine tests were made by studying the maximal and minimal tension, the pulse and the glucosuria following injections of extracts of **thyroid**, adrenal (total, cortex, and medulla), **hypophysis** (total, posterior lobe). The second patient presented hypertrichosis, obesity, mannish appearance and voice, ammenorrhea, imbecility, puerility and alternating periods of excitement and depression. She also had a hyperchlorestinemia and the endocrine tests led to the same diagnosis of an endocrine disturbance of ovarian origin accompanied by disturbances in the lipoid regulation.—F. S. H.

(ENDOCRINE GLANDS) Opothérapie et Endocrinothérapie. Laumonier (J.), Bull. gen. Therap. (Paris), 1920, **171**, 599-612, 637-650.

The author seems to feel that there is a tendency to confound internal secretions and organ extracts. In order to clarify the situation he gives an extensive dissertation on the subject, defining excretion and secretion, and repeating in some detail the well known facts about the conditions attending internal secretion. He then goes on to classify the internal secretions and follows the delineation proposed by Gley, who considers **hormones** those substances which affect function, and **harmozones** those products which affect structure. Of the former **adrenin** is given as a type, of the latter the **thyroid secretion.** To the reviewer, such a classification seems too essentially overlapping to be worth while. In the second part of the discussion organ extracts are differentiated from internal secretions by their toxicity, their similarity of action, the extemporaneous nature and the irregularity of the effect produced, and finally the hemoclasic phenomena attending their administration, all of which may be exhibited when preparations of glands of internal secretion are administered and which are not the properties of any particular tissue.—F. S. H.

(ENDOCRINE GLANDS) Case of myasthenia of thirty years' duration accompanied by bony alterations of the dental maxilla. Progressive evolution (Un cas d myasthénie datant de treize ans avec altérations osseuses maxillo-dentaries a évolution progressive). Lereboullet, Izard & Mouton, Bull. et mém. Soc. méd. d. hôp. d. Par., 1920, **44**, 1618-1623.

An interesting case report but presenting no definite endocrine material.—F. S. H.

ENDOCRINE disturbances (Endokrine Störugen). Lommel. Med. Klin. (Berl.), 1918, **14**, 848.

Report of a case of a 54-year-old man who was suddenly attacked with exhaustion, hypotonia, hyperthermia, marked bradycardia and loss of hair. The disturbances are attributed to a pluriglandular disorder.—F. S. H.

ENDOCRINE GLANDS, Contribution to the study of the dysfunctioning of the— during pregnancy (Weitere Beiträge zum Studium der Dysfunktion endokriner Drüsen in der Schwangerschaft). Mahnert (A.), Arch. f. Gynaek. (Berlin), 1920, **113**, 472-489.

A brief review of the subject and report of experiments made to test the presence or absence of enzymes in the blood of pregnant women capable of affecting **hypophysis** or **pineal** proteins. Abderhalden's micro-method using the refractometer was used. Out of the 25 pregnant women whose serum was examined for the presence of a hypophyseal protein-destructive enzyme 60 per cent gave a positive reaction, from which Mahnert concludes that in the greater number of pregnancies there is a hypophyseal dysfunction. Yet when he finds that out of 20 cases he gets 60 per cent that do **not** give a positive test for pineal protein destruction he also reasons that there is a pineal dysfunctioning in pregnancy.—F. S. H.

(ENDOCRINE ORGANS) Dietetic deficiency and endocrine activity, with special reference to deficiency oedemas. McCarrison (Robt.), Brit. M. J. (Lond.), 1920 (ii), 236-239.

Correction of abstract, Endocrinol., **4**, 641-642. Butter varies in its capacity to protect against edema. This variation is dependent on the quality of the cow's food. Butter is richer in anti-edema substance when the cows are fed on green fodder.—Author's correction.

The diagnosis and treatment of some diseases of the ENDOCRINE GLANDS. Murray (G. R.), Brit. M. J. (Lond.), 1920 (ii), 807-811.

This address deals with the diseases of the **thyroid, pituitary** and **adrenal** glands, special emphasis being placed on the early symptoms of disturbances in function. Besides inspection and palpation, percussion and auscultation very often yield valuable information in an examination of the thyroid gland. Percussion may help to determine the position of the trachea or the presence of gas in a cystic adenoma when infected by a gas-forming organism. Compression of the trachea is indicated by abnormally high pitched breath sounds on auscultation over the trachea. The sounds are

as distinctly audible during expiration as during inspiration. The early symptoms of hyperthyroidism are said to be a constant sense of fatigue, perhaps extending over a considerable period of time; gradual progressive loss of weight, in spite of an increased appetite; change in disposition, restlessness, mental depression or anxiety; fine tremor seen when the hands are extended; slight persistent acceleration of the pulse rate with tachycardia on exertion. There may be slight elevation of the upper eyelids, slight increase in moisture of the skin, disappearance of any former tendency to chilblains and diminution in any tendency to suffer from common colds. An increase in the basal metabolic rate of the patient is a very important symptom (see Endocrinology, 1920, **4**, 71). Rest in bed for several weeks, a liberal diet poor in proteins and x-ray or radium applications are the main points in the treatment of these early cases. Thyroid deficiency in children, in its early stages, is recognized by delay or arrest of growth and lack of normal activity; tendency to coldness of the extremities and dryness of the skin; slight thickening of the subcutaneous tissues, especially of the face, neck, supraclavicular fossae and backs of the hands; slight depression of the bridge of the nose and pale complexion. In the adult, thyroid deficiency is apt to occur between the ages of 40 and 50. The basal metabolic rate falls, there is loss of energy and slowness of the mental processes, and there may be slight myxoedematous swelling of the subcutaneous tissues. The skin becomes dryer and the hair thinner.

Enlargement of the pituitary may cause pressure symptoms such as temporo-frontal headache, diminished fields of vision, epistaxis, etc. The early symptoms of increased function may be drowsiness, sense of fatigue, depression, post-nasal catarrh and photophobia. Finally the well-known skeletal changes appear. X-ray treatment is worth trying; surgical intervention is justified only when the symptoms of intra-cranial pressure must be relieved, otherwise the treatment is symptomatic. Underfunctioning of the pituitary results in the rare condition of adiposo-genital dystrophy. Treatment by pituitary has proved disappointing. In connection with the diseases of the adrenal glands Addison's disease is given the usual text-book description. The remark is made that the administration of 15 minims of adrenin solution in ½ oz. water, 5 to 10 minutes before a meal is very effective in relaxing or preventing spasm of the oesophagus.—L. G. K.

(ENDOCRINE GLANDS) The influence of the spleen, the kidney and of the THYROID in producing anaphylactic crises (L'influenza della milza, del rene, delle tiroide nella produzione della crisi anafilattica). Pistocchi (G.), Pathologica (Geneva), 1920, **12**, 239-240.

Starting from the assertion that anaphylaxis has been of late connected with such morbid conditions as asthma, uremia, eclampsia, epilepsy, etc., and therefore the accessory syndrome must require a ground already prepared, Pistocchi produced experimental alterations of metabolism by removal of the spleen, the kidney or of the thyroid. The removal of the spleen or of one kidney did not appear to alter the anaphylactic reaction, although the experiment was always carried out before the organism could adapt itself to the new condition through a possible vicarious activity of other tissues. Following thyroidectomy the classical symptoms of anaphylactic shock were considerably reduced. The few cases which did not respond in this way are explained by the difficulty of complete thyroid extirpation in the guinea-pig. The author thinks that the delayed metabolism brought about by thyroidectomy probably acts by diminishing the nervous energy, as did the starvation experiments of Besredka.—G. V.

(ENDOCRINE GLANDS) Congenital absence of the vagina and uterus. A consideration of this problem in the light of the more recent endocrine studies and surgical advances, with the report of a case successfully operated upon by the Baldwin method, slightly modified. Robinson (M. R.), Surg., Gynec. & Obst. (Chicago), 1920, **31**, 51-57.

This paper which is largely surgical, emphasizes the point that operative measures tending to create a vaginal tract should be undertaken only in individuals who are physically and psychically women, in the full sense, which this definition implies. In order that the newly constructed vagina should approach the normal as closely as possible it should be lined with a soft, lubricated mucosa, and the employment of an intestinal loop for that purpose, as advocated and executed by Baldwin, is the choice operation. In the author's opinion it is safer to start the separation of the tissues between the rectum and the bladder, in order to establish the copulating channel, from above, instead of from below.—L. G. K.

(ENDOCRINE GLANDS) Vaso-motor disturbances of the nose with special reference to hay fever—with a report for the year 1919. Selfridge, (G.), Laryngoscope (St. Louis), 1920, **30**, 611-625.

The author, although recognizing that hay fever and its allied conditions are the result of protein sensitization, is forced to the conclusion that vaso-motor rhinitis is related to disturbances in the functions of the autonomic nervous system and disturbed endocrine glands. Direct proof is not given for this conclusion, however, a study of asthmatic types and the results of endocrine medication in a limited number of cases would seem to indicate that such cases are the result of disturbed endocrine metabolism. Perhaps, as the author suggests, the reason that certain individuals

become sensitized to proteins is because of an underlying endocrine dysfunction.—H. W.

(ENDOCRINE GLANDS) The heart in endocrine diseases (Herzbefunde bei endokrinen Erkrankungen). Zondek (H.), Berl. klin. Wchnschr., 1920, **57**, 908.

Data reported elsewhere.—J. K.

(GONADS) Homosexuality and hermaphroditism (Omosessualita' ed ermafroditismo). Carrara (Mario), Riforma med. (Napoli), 1920, **36**, 588-589.

This article is a short review of Steinach's studies on the subject, with a report of cases of homosexuals showing ovarian substance in the testes. The author ends by quoting the importance of the phenomena in heredity as demonstrated by Lazzeroni's statistics, according to which the larger part of the sexual inverts beget girls almost exclusively, the few boys that are produced are usually sexual perverts.—G. V.

(GENERAL) Cholesterinemia in normal and pathological conditions (La cholestérinémie a l'état normal et pathologique). Chauffard (A.), Laroche (G.) & Grigaut (A.), Ann. méd. (Paris), 1920, **8**, 60-91.

A cholesterinemia is frequently observed during the first three months of pregnancy, the values then tend to drop only to rise again towards its termination. A similar state of cholesterinemia is also found accompanying menstruation. Its occurrence in **diabetes** is made the subject of a brief comment.—F. S. H.

(GONADS) Eugene Steinach's work on regeneration. Granet (A.), N. York. M. J., 1920, **112**, 612-613.

A review of Steinach's article appearing in Arch. Entwcklungsmech. d. Organ, 1920, **46**, 12.—H. W.

(GONADS) The effects of castration of hen-feathered Campines. Morgan (T.), Biol. Bull. (Phila.), 1920, **39**, 231-247.

Morgan had shown that in the Sebright bantam castration changes the hen-feathered male into a cock-feathered bird. There are only hen-feathered males in the Sebright race. Campines are dimorphic—there being both hen-feathered and cock-feathered males. Hen-feathered males become cock-feathered after castration. The hypophysis seems to be slightly larger in the castrated bird. No change in the adrenals was observed.—W. J. A.

(GONADS) Cytological and experimental studies on sex in Dinophilus apatris (Zytologische und experimentelle Untersuchungen über die Geschlechtsbestimmung bei Dinophilus apatris [Korsch]). Nachtsheim (H.), Arch. f. mikr. Anat. (Bonn.), 1919, **93**, 17-140.

Not of endocrine interest.—W. J. A.

(GONADS) Hypoplasia und tumor. Tschirdewahn. Deutsche med. Wchnschr., (Berl. u. Leipz.), 1920, **46**, 616.

The author demonstrated a tumor of the dimensions of a duck's egg. The patient from whom it was removed had genital hypoplasia, the sex of the patient not being recorded. The tumor was probably partly testicular and partly ovarian.—J. K.

(HYPOPHYSIS) Case of pluriglandular insufficiency (Sobre un caso de insuficiencia pluriglándular). Bosch (B.) & Hernandez (J.), Arch. Conf. Medicos Hospital Ramos Mejia (Buenos Aires), 1919, **vii**, 87.

Observations on a case of dystrophia adiposo-genitalis.—B. A. H.

Action of HYPOPHYSEAL injections in certain syphilitic migraines and in the ordinary congestive headaches (La accion de las inyecciones hipofisarias sobre ciertas cefaleas sifiliticas y sobre las cefaleas congestivas banales). Bouveyron. Bull. de la Soc. Francaise de Dermat. et de Syphilograph (Paris), 1920, **vii**, 283-285.

Bouveyron used the intramuscular injection of posterior lobe extracts in amounts corresponding to 20 centigrams of the ox pituitary, in syphilitics with roseola and intense headache and found that all symptoms disappeared within five minutes. The roseola reappeared, however, within an hour, but the headache did not recur for two hours. If hypophyseal extract injections are made at the same time as the intravenous injection of arsenobenzol, not only are the exacerbations of headache produced by the arsenical, impeded but that already present is diminished. The extracts were also used with success in preventing the accidents of congestion accompanying the administration of arsenobenzol. Report is made of a case of bilateral tonsilitis, with a temperature of 39 degrees C., in which the headache was very severe. The latter was ameliorated in five minutes after the exhibition of pituitary extract; on the other hand, the temperature rose to 40 degrees C. in fifteen minutes. This case does not demonstrate whether the headache was of thermal or toxic origin, but does show that temperature and headache are dissociable phenomena.

It would appear as if the greater number of headaches is produced by an intracranial hypertension from the fact that they are alleviated by lumbar puncture and because in cerebral tumors, accompanied by intracranial hypertension, headache is a rather constant symptom.

The results of hypophyseal injections seem to favor this conception, according to the author, who concludes by stating that such injections can serve as a means of diagnosis of congestive headaches.—C. G. C.

(HYPOPHYSIS) Complete recovery from Djabetes Insipidus. Cammidge (P. J.), Practitioner (Lond.), 1920, **105**, 244-247.

A case is reported in detail of complete recovery without relapse for 6 years following lumbar puncture. Various diets had been instituted, antisyphilitic treatment had been tried, pituitary injections administered, but only with temporary improvement. About one ounce of spinal fluid was then withdrawn under considerable pressure. Cammidge suggests that para-syphilitic changes at the base of the brain interfered with the passage of the hypophysis secretion into the cerebro-spinal fluid and sudden release of pressure by lumbar puncture broke down adhesions and opened a channel for its normal passage again. Herrick reported a similar cure in Arch. Int. Med., July, 1912. —H. L.

(HYPOPHYSIS) Case of acromegaly (Sobre un caso de acromegalia). Chiappori (R.) & Gonzalez (T.), Arch. Confer. Medic. Hosp. Ramos Mejia. Semana Med. (Buenos Aires), 1919, **26**, pt. 2, 242.

Observation of a case with hemianopsia and mild glycosuria. —B. A. H.

(HYPOPHYSIS) Radiographs of the sella turcica (Radiografias de la silla turca). Donovan (C), Rev. de la Asoc. med. argent. (Buenos Aires), 1920, **32**, 234-238.

Technical considerations and descriptions of radiography of the sella turcica.—B. A. H.

(HYPOPHYSIS) Case of acromegaly. Faber (K.), Ugesk. f. Laeger (Copenhagen), 1916 **78**, 613-615.

Faber presents a patient with acromegaly in an early stage. The patient showed coarse, plump features, diastasis between the teeth, while the x-ray showed an enlargement of sella turcica. No change of the visual field and no optic atrophy or neuritis was present. The patient was subjectively improved after **thyroid** treatment. In the discussion Lauritzen mentioned two cases in which acromegaly was combined with goiter, one of which was also a severe diabetic.—K. H. K.

(HYPOPHYSIS) Case of Fröhlich's syndrome (Sobre un caso de sindrome de Fröelich). Garcia Lagos (C.), Semana méd. (Buenos Aires), 1918, **25**, pt. 2, 21.

A case report with no novel data.—F. S. H.

Influence of x-rays on the HYPOPHYSIS (Ueber Hypophysenbestrahlung). Geller (F. C.), Inaug. Disst., Breslau, 1920, Asbt. Zentralbl. f. Chir., 1920.

The hypophysis of young female rabbits was exposed to x-rays. The growth of the organ, especially of the middle and anterior lobe was retarded. The small cells which probably are the juvenile form of the large chromophil cells proved to be very sensitive to x-ray. The growth of the animals was less than the controls. No influence on the ovaries was observed.—J. K.

(HYPOPHYSIS) Report of a case of encephalitis lethargica in a pregnant woman with autopsy findings. Haag (M. D.), J. Mich. M. Sc. (Grand Rapids), 1920, **19**, 483-487.

The anterior lobe of the pituitary showed marked congestion, infiltration and hypertrophy of the basophilic cells.—H. W.

(HYPOPHYSIS) The therapeutics of the pituitary extract. Herman (G. J.), Kentucky M. J. (Bowling Green), 1920, **18**, 381-383.

Brief review of the subject; nothing new.—H. W.

Syphilis of the brain with changes in the HYPOPHYSIS (Hirnlues mit Hypophysenveränderung). Josephy, Deutsche med. Wchnschr. (Berlin), 1920, **46**, 1323.

Data published elsewhere.—J. K.

(HYPOPHYSIS) Acromegaly. Kraus (E. T.), Berl, klin. Wchnschr., 1920, **57**, 908.

The autopsy of this case showed an eosinophil adenoma of the **hypophysis**; struma nodosa. The heart weighed 950 grams, the liver 3220 grams, the spleen 650 grams, the **thyroid** 150 grams, the **pancreas** 150 grams, and the **adrenals** 25 grams. The **pineal, parathyroids, thymus,** and **testicles** were of normal weight.—J. K.

Further evidence on the functional correlation of the HYPOPHYSIS and the THYROID. Larson (J. A.), Am. J. Physiol. (Balt.), 1920, **53**, 89-100.

A repetition of the work presented in a former paper, with a larger number of animals and with strict regard to the comparison of individuals from a single litter. (See Endocrin., 1919, **3**, 534.) The original results are confirmed.—T. C. B.

(HYPOPHYSIS) Infantilisme hypophysaire et sifilis. Léreboullet (P.) & Mouzon (J.), Rev. neurol. (Paris), 1917, **24**, 493-497.

A description of a rare case of causal association of syphilis with infantilism of hypophyseal origin presenting the classical picture of

the latter disturbance such as adiposity infantile genitalia, bilateral optic atrophy, right temporal hemianopsia, etc. The x-ray showed a large sella turcica, but with no definite pathological characters. Lumbar puncture showed a high pressure and the fluid contained 0.06 per cent albumen and 12 lmyphocytes per cc. The Wassermann was negative. There were no symptoms of **hypothyrodism.** Antisyphilitic treatment was begun but as yet no conclusion can be given of the results of such endeavor.—F. S. H.

(HYPOPHYSIS) Pituitary tumor-operation by transsphenoidal route. Lewis (F. O.), Penn. M. J. (Athens), 1917-18, **21,** 282-284.

Report of a case of hypopituitarism with a tumor of the hypophysis which was successfully removed by operation, the patient dying the next day.—F. S. H.

Comparative vascular action of HYPOPHYSIS extract and histamine associated with ADRENIN (Accion vascular comparada de la histamine y del extracto de hipofisis asociadas a la adrenaline). Llosa (J. B.), Rev. de la Asoc. med. argent. (Buenos Aires), 1920, **32,** 62-63.

While hypophyseal extract reinforces and prolongs the action of adrenin on blood-pressure, histamine has an antagonistic action in all doses.—B. A. H.

Deep x-ray therapy in tumors of the HYPOPHYSIS. Loeb (C.), Am. J. Ophth. (St. Louis), 1918, **1,** 397-403.

This is a review of previously recorded cases, with a report of a case greatly benefited by deep x-ray therapy, and a comparison with a case relieved by operative treatment. The x-rays were applied over the right and left temple, right and left antrum, and nose. Between the skin and the tube, an aluminum plate of one millimeter thickness was interposed to cut out some of the soft rays. The applications were made until an erythema dose had been given. In the beginning this was given in four applications of five minutes each, in ten days to each area. Later the amount given was one-fifth less. The skin focus distance was eight inches. The equivalent spark gap of the tube varied from nine to fourteen inches, usually eleven inches. From 3-5 milliamperes to 1 4-5 amperes were passed for four to six minutes, producing in each treatment three seven milliampere minutes. Relief was obtained.—F. S. H.

(HYPOPHYSIS) Case of acromegaly of apparently acute onset. Loewenberg (S. A.), Internat. Clin. (Phila.), 1918, 28, **3,** 154-157.

A complete case report with good illustrations presenting no new data save the appearance of the clubbing of the finger-nails and the acute onset of the enlargements of the fingers and toes.—F. S. H.

(HYPOPHYSIS) Clinical contribution to the knowledge of the pathogenesis and therapy of diabetes insipidus (Contributo clinico alla conoscenza della patogenesi e terapia del diabete insipido). Nasso (I.), La Ped. (Napoli), 1920, **28,** 812-816.

Nasso reports a case of a girl of 7 years with a positive Pirquet and slight jaundice, who for the last 4 years was accustomed to drink from 11 to 14 quarts of water daily, passing from 12 to 15 quarts of urine each day. The appetite was apparently unimpaired. When intramuscular injections of pituitary extract were made the water ingestion was reduced to 3 or 4 quarts and the urine excretion to 4 or 5 quarts a day. The fact is worth noting that the patient was eliminating more than she was drinking, and yet there was no loss of body weight. The condition is attributed to hypopituitarism.—G. V.

(HYPOPHYSIS) Encephalitis lethargica. Schwartz (S.), N. York M. J., 1920, **112,** 182-185.

Encephalitis lethargica is the result of perivascular infiltration of the pons and medulla. The hypophysis because of its infundibular connection with the base of the brain may become involved in a like manner. That the lethargic condition, at least in part, involves the hypophysis is shown by the relief following the administration of anterior lobe extracts. The lethargy in such cases bears no relation to the amount of infection and focal symptoms (lethargy) set in only when the hypophysis becomes involved in the process of perivascular infiltration.—H. W.

(HYPOPHYSIS) Use of intravenous injections of pituitrin, especially in hemorrhage during the various periods of labor. Tofte (A.), Ugesk. f. Laeger (Copenhagen), 1916, **78,** 745-751.

Tofte has seen good results following the intravenous injection of pituitrin (Parke, Davis & Co.) in cases in which subcutaneous injection has been without effect. The intravenous injection may be used in every stage of labor but the main indications are: 1. Cases of placenta praevia partialis with the foetus in head-position. 2. A retention of the placenta, when Crede's expression is without effect. 3. In cases in which it is of advantage to produce a sudden and active labor, e. g.: after reposition of arms or legs. 4. In cases in which labor is to be helped but the subcutaneous or intramuscular injection is without effect. Heart and kidney diseases are not absolute contraindications against the employment of pituitrin.—K. H. K.

INFANTILISM: Brissaud and Fröhlich types. Griffith (J. P. C.), N. York M. J., 1918, **108,** 529-530.

Data reported in Endocrinology **2,** 507.—F. S. H.

The diagnostic use of the INTERNAL SECRETIONS in diseases of digestion and nutrition (Die diagnostische Verwertung der Lehre von der inneren Sekretion für die Klinik des Verdauungs-und Stoffwechselkrankheiten). Biedl (A.), Deutsche med. Wchnschr. (Berlin), 1920, **46**, 1380.

Most cases of adiposity are of endocrine origin. Their diagnosis is only made "ex juvantibus." Abnormal leanness is generally due to hyperfunction of the endocrine organs. In these cases radium or x-ray treatment may prove useful if care is taken that no destruction is caused. Senile symptoms are not due only to the loss of function of the **sex glands.** All endocrine organs may play an important part in senescence. The author observed a child with senile symptoms which was cured by **thyroid** and **hypophysis** treatment. The thyroid treatment is of use in cases of obstipation; the **adrenals** seem to play a part in the pathogenesis of ulcers of the stomach, also the endocrine organs seem to be of great importance in the pathogenesis of malignant tumors.—J. K.

The principles of INTERNAL SECRETION. Brown (W. L.), Brit. M. J. (Lond.), 1920, **(ii)**, 687-691.

Much of the content of this address is of a speculative nature, and it is difficult to see the relation between some of the generalizations laid down in the introduction and the subsequent portion of the paper. For instance, it is stated that the more widely tissues differ the more they can make use of the end-products of each other's metabolism —as evidenced by plants and animals. Also in general terms the more similar are the tissues the less can they make use of each other's end-products of metabolism. They require specially elaborated secretions (hormones) to produce beneficial actions. The similarity of vitamines to hormones is claimed, as shown by their effectiveness in minute doses, their chemical similarity and the resemblance of the results produced when either is lacking. Thus rickets and osteomalacia, the neuritis of beri-beri and the neuritis of **diabetes,** scurvy and the form of purpura due to **adrenal** deficiency are said to be very similar diseases. Another generalization made, is that the sympathetic, since it is the most primitive part of the nervous system, is closely associated with the endocrine system, a still more elemental means of communication in the body. Also since specialized reproductive cells appeared before the nervous system the organs of reproduction also remain closely associated with the older chemical reactions now specialized in the endocrine glands. "The endocrine glands, the reproductive organs, and the sympathetic nervous system, therefore, remain as a basic tripod, a..d it is not likely that a disturbance will occur for long in one limb of this tripod without affecting the other two."

The disturbances of the various ductless glands are then considered in detail, with emphasis on some of the minor degrees of derange-

ment which usually escape unnoticed. Adrenin exhaustion is given as a possible reason for many war neuroses and other functional changes characterized by lack of vascular tone, vasomotor instability and myasthenia, especially when accompanied by a low blood pressure. Hertoghe's views, that minor degrees of **thyroid** insufficiency produce such symptoms as relaxation of the articular ligaments, particularly in the knee, ankle and thoracic vertebrae, causing knock-knee, painful heel, flat-foot and lordosis, are quoted. Infiltration of tendons and fascia producing rheumatoid pains; loss of hair in the outer half of the eyebrow, enuresis, diminished coagulability of the blood, and infiltration of the nerve centres causing mental slowness, loss of memory, etc., are similarly attributed to deficient thyroid secretion. Minor degrees of **hypo-pituitarism** are said to occur in which the condition of the skin and subcutaneous tissue recalls myxoedema, but the mental state remains active. The obesity is marked. Polycythemia is of frequent occurrence. These three glands are mainly catabolic. "They throw sugar into the blood stream for active consumption, they co-operate with the sympathetic in defensive activities, they divert the stream of energy outwards, they are accelerators." On the other hand, the endocrine elements of the stomach, duodenum and **pancreas** and the **parathyroid** glands are mainly anabolic in function. These co-operate with the parasympathetic, they divert the stream of energy inwards and store potential energy. They are retarders.

Finally the general principles of internal secretion are set forth as follows: Fertilization of the ovum initiates a tremendous impulse to growth. When growth is expressed as a fractional increase of body weight it will be found that its curve continuously diminishes from fertilization onwards. In other words, the impetus gradually wears out. But the organism is supplied with intrinsic regulators (the endocrine glands and their associated nervous mechanisms) acting as retarders or accelerators. In the first few years of life the original impetus is so enormous that a break is needed, which seems to act through the **thymus.** (The author has previously admitted that the thymus probably does not supply an internal secretion.) By seven years of age this break is no longer needed, and should it continue to be applied from any cause, infantile features persist. With the aid particularly of the thyroid and pituitary, active growth continues till a new equilibrium must be found with the development of a new set of glands at puberty. The climacteric gives another jolt to the mechanism and from this point on the dying down of the original velocity is marked. Finally the author points out that before we can apply organotherapy rationally we must have some clear idea of the chemistry of the hormones.

(The author shows by such a statement as "since the sympathetic nervous system depends on adrenalin for its activity," that he is not

familiar with or discards recent physiological work on this subject.)—L. G. K.

Psychosis and INTERNAL SECRETION (Psychose en inwendige afscheiding). de Hartogh (J.), Nederl. Tijdschr. v. Geneesk, (Haarlem), 1920, **64**, 2465-2471.

The author reports a case in which the good influence of **corpus luteum** on psychical complaints was observed. The theories are, however, very superficial. According to the author it is well known that **thyroid** hyperfunction produces Graves' disease, hyperfunction of the **adrenals** produces tumors, hyperfunction of the **parathyroids** myasthenia pseudo-paralytica and hypofunction of the **hypophysis** dystrophia adiposo-genitalis. The author states also that we know (?) that the **thymus** produces a hormone stimulating the vagus and the growth of the bones. However, very little is proved of all these statements. The article is an example of that sort of dilettantism with which endocrinology is especially afflicted. —J. K.

(INTERNAL SECRETIONS) Organ extracts as aids in labor (Organextrakte als Wehenmittel). Köhler (Robert), Monatschr. f. Geburtsh. u. Gynäk. (Berl.), 1920, **52**, 240-247.

This study is concerned with the effects that have been produced by the injection of **placenta** extracts at the end of pregnancy (19 cases), at premature deliveries (7 cases), and in attempts to induce abortion (4 cases). In all of these positive results were obtained, in that within an hour, usually in nine or ten minutes, after the injection of the extract the first labor pains appeared, and gradually increased till delivery occurred. In some cases a single injection was insufficient, but a second dose started the processes on their way again. In four cases operative interference was necessary. The breasts usually become full of milk the usual time after parturition and lactation was successful. These results confirm others by the same author in which he used extracts of many different tissues and he consequently comes to the conclusion that the effect produced is not specific to the placenta nor to any other tissue, but is a common property of all organ extracts when prepared as described.—F. S. H.

(INTERNAL SECRETION) Further investigations on the origin of tumors in mice. VI. Internal secretion as a factor in the origin of tumors. Loeb (J.), J. Med. Research (Boston), 1919, **40**, 477-496.

The **ovarian** hormone (not pregnancy, suckling, etc.), is considered responsible for differences in the breast cancer of male and female mice. Specific hormones are also postulated—that is, they influence cancer in organs to which they are normally related; for

example, **breast** and ovary, **uterus** and ovary, **prostate** and **testis.** In the development of cancer there are three factors—heredity, irritation and effect of hormones; heredity and internal secretion act together; heredity may be associated with irritation, but irritation by itself, if strong enough, may cause cancer. Physiol. Abst. **5**, 490.

INTERNAL SECRETIONS in the organism of tubercular tendencies. Observations in the army (Las secreciones internas y el terreno organico tuberculizable. Observaciones en el Ejercito). Lopez (Julio A.), Semana méd. (Buenos Aires), 1920, **27**, 586.

Disturbances in the internal secretions are said to be the cause of the tendency to tuberculosis.—B. A. H.

INTERNAL SECRETIONS, and uremia (Urémie et sécrétions internes). Remond (A.), Bull. Acad. de Med. (Paris), 1917, **77**, 174-177.

A series of experiments on rabbits. In each series but one experimental animal and one control animal was used. A comparison was made of the amount of human serum obtained from a patient suffering from Bright's disease, that would kill a rabbit after having been treated for several days with **thyroid** extract, and the amount that would kill an untreated animal. Other experiments are reported of the length of time rabbits lived after being given sodium cantharidate in the ratio of 1 to 500 per kilo body weight with and without preliminary treatment with **thyroid** extract, 1 animal; **adrenal** extract, 2 animals; renal extract, 1 animal; renal plus adrenal extract, 1 animal; thyroid plus parathyroid, 1 animal; and 3 animals received thyroid plus parathyroid after the sodium cantharidate. Although there were uniform changes in the thyroid of a severe nature in those rabbits which died first, it is the opinion of the reviewer that the small number of animals used in each different series makes any conclusions of very doubtful value.—F. S. H.

(INTERNAL SECRETIONS) Chronic acrocyanosis (Acrocianosi cronica). Zagari (G.), Riforma med. (Napoli), 1920, **26**, 709-715.

This article is a report of a clinical lecture during which 2 different cases of acrocyanosis were demonstrated. Both of the cases belonged to Cassirer's classification. After discussing the syndromes according to the classification in, (a) vasomotor acropathies from peripheral angiospasm; (b) vasomotor acropathies connected with angioparesis; (c) angiotrophic acropathies (some cases of sclerodermia), he places his cases into the third class. In the discussion there is brought out the great part played in these disorders by the endocrine-sympathetic and the sympathetic system, though the possibility of the existence of cases independent of endocrine dysfunction is admitted. The first case, in which the disturbance was purely local, did not

belong to the group in which endocrine dysfunction is manifest. The second case, in that x-ray examination showed the phalanges to exhibit a previously existant acromegaly, was put in the class where endocrine dysfunction plays a role. Since the author is uncertain as to which gland is disturbed he intends to begin with thyroid treatment, inasmuch as all such cases seem to depend more or less on alterations in the function of this gland.—G. V.

INTERNAL SECRETIONS and the heart (Herz und innere Sekretion). Zondek (H.), Zeitschr. f. klin. Med. (Berlin), 1920, **90**, 171-197.

According to Zondek the heart shows the following symptoms in myxedema:.

A. Before treatment with **thyroidin:**

1. Dilation of the right and left heart. Often the aorta is enlarged. 2. The heart beats slowly; the blood pressure is normal. 3. An x-ray photograph shows the outlines of the heart more clearly than in the picture of a normal heart. 4. The atrial wave and the A wave in the electrocardiogram are lacking. In the phlebogram the A wave is also lacking. A detailed description of the electrocardiogram is given with illustrations.

B. After treatment with **thyroidin:**

1. The heart returns to its normal size again. Generally the aorta remains enlarged. 2. The pulse rate becomes normal; the blood pressure does not change. 3. The electrocardiogram and the phelbogram become normal in contour. When the P and Z waves become abnormally high this is a sign that the treatment must be stopped at once. Both in ordinary obesity and in thyrogenous obesity there is generally more or less cardiac dilation without changes in the blood vessels. The blood pressure is sometimes low in the latter. The changes in the skiagram and electrocardiogram as seen in myxedema are never observed in other cases of hypothyroidism (cretinism, alopecia, etc.). In infantilism there is often vascular and cardiac hypoplasia with a low pressure.—J. K.

Two cases of LIPODYSTROPHIA PROGRESSIVA. Neel (A. V.), Hosp.-tid. (Copenhagen), 1916, **59**, 1253-1265.

Two cases of this disease are described by the author. No history of inheritance is given in either case and the general health appeared to be good. The first case was a woman of 52 years. Her periods began at the age of 18 and lasted until she was 47 years old. At the age of 40-42 years a marked emaciation of the face occurred which was followed by emaciation of the chest and arms. The legs and hips had always been very large and did not change in volume along with the other changes. Some slight complaint of headache was made, but

nothing more. A tumor which was situated on the right arm and was probably a lipoma, did not decrease in size with the emaciation of the upper limbs. The x-ray examination showed nothing abnormal. The blood examination showed the presence of a lymphocytosis. Eight similar cases have been previously described. The second case was a woman of 30 years who up to the time she was 19 years old had been full-faced and stocky in the upper part of her trunk. From that time on she began to become emaciated in these parts while from the age of 14 years on a progressive adiposity of the legs and hips had taken place. The skin of the face appeared as that of a myxedematous person. The hands were large, with short, broad fingers. Pubic hair was scanty. The uterus on palpitation appeared to be small and infantile, while the ovaries could not be felt. The author is of the opinion that that lipodystrophia is of endocrine origin.—K. H. K.

MENSTRUATION and its anomalies (Der Menstruationzyklus und seine Anomalien). Schröder (R.), Monatschr. f. Geburtsh. u. Gynäk. (Berl.), 1920, **53**, 207-251.

A bibliographical review.—F. S. H.

Case of MYOTONIA. Jewesbury (R. C.), Proc. Soc. Med. Lond. 1918, **11**, Sect. Stud. Dis. Child., 58-60.

Not of explicit endocrine interest.—L. G. K.

Über OSTEOMALAZIA. Koltonski (Hermann), Monatschr. f. Geburtsh. u. Gynäk. (Berl.), 1920, **52**, 253-262.

The fundamental cause of osteomalacia is attributed to a disturbance of the endocrine system of some sort. The **ovaries** cannot be concerned inasmuch as the disorder occurs in man as well as in woman. Admitting that there is a pluriglandular disorder frequently made evident the author is inclined to the opinion that an adrenal hypofunction is at the basis of the disease.—F. S. H.

OSTEOMALAZIA. Wagner (G. A.), Berl. klin. Wchnschr., 1920, **57**, 934.

A report of a woman of 46 with typical osteomalacia and with **thyroid** atrophy who had never menstruated. The explanation that osteomalacia is due to hyperfunction of the **ovary** is not supported by this case. **Adrenin** had no effect, while phosphorus and cod liver oil produced some improvement.—J. K.

(OVARY) A case of OSTEOMALACIA treated by oöphorectomy. Hellier (J. B.), Brit. M. J. (Lond.), 1920, **(ii)**, 587-588.

The patient was a woman, 38 years of age, who had had four pregnancies. She did not regain her strength properly after the birth of her second child, five years previously. Eighteen months before she

was seen by the author she had an abortion in the second month of gestation. She had lost weight and had numerous pains all over for five years, and was able to walk only with difficulty. Both clavicles broke spontaneously during her fourth pregnancy, and in the seventh month she developed albuminuria and marked anasarca up to the level of the scapulae. There was a bed sore over the sacrum and the left leg was very painful. She had spinal curvature and marked contraction of the pelvis and rostration of the symphysis. Labor was induced, but craniotomy was necessary on account of the lateral contraction of the pelvis. About a month later, when first seen by the author, the albuminuria had disappeared, but the osseous system showed many anomalies—deformity of the pelvis, kyphosis, lordosis, and fracture of the femur. An x-ray examination showed the bones to be so little opaque that it was impossible to obtain a good skiagram. Both ovaries were then removed at operation; they were normal in appearance. Twelve months later the patient was much improved. She was able to walk some distance without crutches, and her pain had disappeared. The skiagram showed the bones to be more opaque and there seemed to be some new bone formation at the iliac crests. The remark is made that 80 per cent of osteomalacia cases recover under this treatment.—L. G. K.

The influence of the OVARIAN hormone on the growth of the pelvis (Über den Einfluss des Ovarialhormons auf das Beckenwachstum). Plaut (Rachel), Ztschr. f. physiol. Chem. (Berl. u. Leipz.), 1920, **111**, 36-42.

The question of whether or not the pelvic form is dependent on any function of the gonadal cell activity is discussed in this paper. Plaut injected into rabbits an oil suspension of an ether extract of ovaries containing corpora lutea of cattle, guinea-pigs and cats. Each dose was the equivalent of one ovary, and one dose was given daily for from ten to fourteen days. The oil was poorly absorbed. After waiting another fourteen days the animals were killed and the pelvic measurements were compared when possible with controls from the same litter; when not possible animals of the same age, sex and size were used. The results indicate that the extract as prepared from corpora lutea containing ovaries causes a transverse enlargement and a longitudinal diminution of the pelvis of both sexes.—F. S. H.

(OVARY) The physiology of ovulation. Schochet (S. S.), Surg. Gynec. & Obst. (Chicago), 1920, **31**, 148-149.

This is a preliminary report only, in which the author states that ovulation is due to a specific enzyme in the liquor folliculi, its nature being similar to the enzyme erepsin. Apparently there are other proteolytic enzymes in the liquor folliculi; also a lipase. Atresia of the follicles is due to this enzyme or enzymes. These experiments are

said to offer a rational explanation for the use of **thyroid** extract and **corpus luteum** in sterility.—L. G. K.

(OVARY) The physiological chemical action of follicular extract (Die physiologisch-chemische Wirkung des Follikelsaftes). Wintz (H.), Arch f. Gynaek. (Berlin), 1920, **113**, 457-471.

Among a great number of experiments carried out in the study of the internal secretion of the ovary a certain number were done in which the effects of the follicular extract were tried on blood-pressure, blood coagulation and local action on the genitals. Using rabbits as the experimental animals, small doses given intravenously caused a fall in blood pressure, while large doses gave the opposite reaction, though neither of the reactions were very marked. When the extract was injected in the ear vein and blood taken two minutes later and tested for coagulation time, it was found that this phenomenon was slightly but significantly lengthened. No effect on the genitalia was observed. No effect of the extract could be observed on the coagulation time of blood in man, nor was menstruation either augmented when slight or diminished when profuse, as the result of the injection of such extracts in 1.5cc. amounts. These experiments were all done when extracts from fresh tissue were used. When old tissue extracts were tried there was obtained a rise in blood pressure even with small amounts, there was a shortening of blood-coagulation which, however, was a transitory phenomenon, and no action on the genitalia was observed.

When **corpus luteum** extracts were similarly studied they were found to produce a fall in blood-pressure, a slowing of blood-coagulation and an hyperemia of the genitalia. (This, however, only occurs after some 30 days' injections.) A review is then given of the action of lipamin and luteolipoid preparations obtained from the corpus luteum. The former causes a slight drop in the blood pressure, while the latter has no effect. Lipamin retards the coagulation of blood, while luteolipoid accelerates it markedly.

Moreover, luteolipoid but slightly accelerates the growth of the genitalia of virgin rabbits, while the lipamin effect on the uterus and mammae is most marked. Luteolipoid when injected during the menstrual period is an efficient inhibitor, save in those cases due to endometrial pathology. Lipamin when injected in patients with amenorrhea yields relief, but has no effect on a normally menstruating woman.—F. S. H.

(PANCREAS) The blood and urine in pancreatic disease. Cammidge (P. J.), Forsyth (J. A. C.) & Howard (H. A. H.), Lancet (Lond.), 1920, **(ii)**, 393-401.

In a series of clinical observations supported by animal experiments on dogs and rabbits the authors show that the dextrin content of the urine and blood is considerably increased in pancreatic disease

even before glycosuria occurs. This dextrin is said to be an intermediate product between the hepatic glycogen and sugar. Special methods of estimating the dextrins in the blood and urine are described. The amylolytic ferment of the blood and urine is also increased in diseases of the pancreas, varying directly with the percentage of sugar in the blood after a meal and inversely as the dextrin content of the blood and urine. In the animal experiments it was shown that the greater the amount of pancreatic tissue removed, and consequently the more marked the hyperglycaemia and glycosuria, the less is the dextrin content of the blood. It was concluded that the internal secretion of the pancreas exerts a restraining influence on the glycolytic (glycogenolytic) ferment of the liver, since, following an injection of an extract of pancreatic tissue, the percentage of sugar and of dextrin in the blood is considerably reduced. A relative diminution in the secretion of the pancreas, with consequent greater liberty of action on the part of the glycolytic (glycogenolytic) ferment of the liver, gives rise in the early stages to an increased formation of the intermediate products of glycogen degradation without any change in the sugar, and in the later stages to an increasing sugar production with a proportional diminution in the intermediate products. The appearance in the blood and urine of these intermediate products of carbohydrate metabolism (dextrins) indicate a pre-diabetic condition which, if allowed to go unchecked, will be followed by hyperglycaemia and glycosuria. Incidentally it is shown that a considerable proportion of a well-boiled starch is absorbed into the portal circulation in the form of dextrins and maltose, whereas an uncooked starch enters the portal blood chiefly as glucose.—L. G. K.

Experimental studies of the internal secretion of the PANCREAS (Experimentelles Studium der inneren Sekretion des Pankreas). Kumagai (T.) & Osato (S.), Tohoku J. Exp. Med. (Sendai), 1920, **1**, 153-166.

The object of this study was to determine whether the internal secretion of the pancreas is discharged directly into the blood vessels or into the lymphatics and thence into the blood vessels by the thoracic duct. The evidence advanced is as follows: (1) Transitory glycosuria developed in all of four dogs with thoracic duct fistulae, but only in two of twelve dogs in which the duct has been simply ligated. (2) Subcutaneous injection of thoracic duct lymph in dogs with all pancreatic tissue removed has no effect upon sugar excretion, but a uniformly positive effect was noted in animals following partial removal of the pancreas. (3) In two dogs injected with pilocarpin the amylase in the lymph is increased above that in the blood, while in the normal condition it is less. (4) In two other dogs the authors found that the injection of lymph from pilocarpinized animals has an antiglycosuric effect. The authors accordingly conclude that the in-

ternal secretion of the pancreas is passed first into the lymphatics and thence in the blood stream.—E. V. C.

(PANCREAS) Test for the digestion of nuts and diagnosis of pancreatic insufficiency (L'epreuve de la digestion des noyaux et le diagnostic de l'insuffisance pancréatique). Labbé (M.), Ann. Méd. (Paris), 1920, **8**, 101-115.

Not of endocrine interest.—F. S. H.

Development of liver, PANCREAS and fore-gut in the duck and the mole. (Zur Entwicklungsgeschichte der Leber, des Pancreas und des Vorderdarms bei der Ente und beim Maulwurf. Ludwig (E.), Anat. Hefte (Weisb.), 1919, **56**, 513.

Of embryological interest. Not much space is given to the pancreas.—W. J. A.

PANCREAS, Accessory pancreas in the dog. Mann (F.), Anat. Rec. (Phila.), 1920, **19**, 263-268.

An accessory pancreas was observed in a dog during experimental operation. It was located below the ligament of Treitz. On histological examination it appeared normal, possessing acini, ducts and many small islets.—W. J. A.

The PLACENTAL gland and placental extract. Bandler (S. W.), N. York M. J., 1920, **112**, 745-750.

Placental extracts tend to diminish uterine bleeding and are second only to **mammary** extracts in controlling excessive menstruation, though they lack the power of the latter of diminishing the size of the uterus. Placental extract often prevents threatened miscarriage or abortion, especially if given along with **thyroid** extract. The psychic symptoms of restlessness and mental irritability which result because of an over-activity of the posterior **pituitary**, are quieted by placental extracts. The instincts of libido sexualis can be controlled or modified by the administration of placental extracts, especially in conjunction with extracts of the **thymus.** The importance of the placenta and placental extracts is the ability to influence the posterior pituitary and to stimulate the **anterior pituitary** and the **adrenal cortex.** Prior to the presentation of the above observations the author goes to some length in presenting his views concerning the interrelation of the endocrine system in the female. The gist of his theory is given in the following quotation: "The production of menstruation is initiated by the **ovary**, not forgetting the interstitial structure. Co-operation is evidenced by the **corpus luteum** and thyroid and posterior pituitary. Unless the posterior pituitary is inhibited, menstruation takes place. * * * It would seem as if all those activities suggested and started in each

premenstrual phase are then accentuated and made into a definite balance for nine months by the introduction of the placents. The balance in the autonomic nervous system which takes on the form of a crisis at menstruation is altered by placental action and is postponed to the day of labor. In pregnancy the entrance of the anterior pituitary and particularly of the adrenal cortex is assured or produced by the placenta."—H. W.

PARATHYROID transplantation; how to choose the material for transplantation (Epithelkörperverpflanzung; die Wahl des Transplantates). Borchers (E.), Zentralbl. f. Chir. (Leipzig), 1920, **47**, 1366-1368.

The question whether transplantation of the parathyroids is useful in tetany, especially in the postoperative form, is still largely discussed. The investigators, however, do not agree. Borchers tried to find the reason of the different results of different workers. One of the differences may be due to the way the surgeon treats the parathyroid. This tissue must be handled with extreme care. But there is a much more important factor. Most organs transplanted as parathyroids are not parathyroids. In 11 cases the author himself removed during an operation for goitre a parathyroid for transplantation. The organ was situated in its typical location. Before transplanting a small piece was taken for histological examination. Of these 11 organs only one proved to be a parathyroid; 8 times it was an accessory thyroid, once a lymph gland and once a little piece of fat. To avoid such results the author advises the following technic. During an operation for goitre in man (it is preferable that the goitre is not too large) a parathyroid (or the organ that is believed to be one) is removed and kept in sterile physiological solution at 37 deg. C.; a very small piece is taken, fixed in boiling formalin, cut with the freezing microtome, and examined in glycerine. This takes no more than 10 minutes. If the organ proves to be a parathyroid it is transplanted at once into the left musculus obliquus intermus abdominis of the tetanical patient.—J. K.

(PARATHYROIDS) Experimental studies on tetany (Experimentelle Untersuchungen über Tetanie). Farner (E.) & Klinger (R.), Mitt. a.d. Grenzgeb. d. Med. u. Chir. (Jena), 1920, **32**, 469-497.

In the cat nearly always small accessory parathyroids may be found in the thymus itself or its surrounding connective tissue. The authors removed in 40 cats the four principal parathyroids. The effect was not the same in all animals. Often an acute or sub-acute tetany developed which frequently ended fatally, but many animals remained in good health after the operation. This is probably not due to the remaining accessory glands as there was no correspon-

dence between the existence of such glands and the symptoms. When soluble calcium salts are given these have a good influence on the symptoms. Twice the authors tried transplantation of a parathyroid to cure the postoperative tetany. In both cases temporary improvement was seen. Administration of **thyroid** had no or at most an unfavorable effect. Noël Paton has shown that guanidine or methylguanidine when given to animals, produces symptoms closely resembling tetany. The authors consider tetany as an intoxication with guanidine compounds. The function of the parathyroid would be to destroy (probably to oxidize) these substances. The good result following calcium treatment would be due to the fact that calcium salts give a precipitate with guanidine compounds. The intensity of tetany would depend upon the quantity of parathyroid tissue and the quantity of guanidine compounds in the body.—J. K.

The PARATHYROID and convulsive states. Jelliffe (S. E.), N. York M. J., 1920, **112**, 877-879.

Convulsive states may be looked upon from a neurological standpoint as the result of a lowered or altered function of the synapses. The action of the normal parathyroid gland appears to control or steady synapse function, possibly because of its control over calcium metabolism. The administration of parathyroid preparations by way of the rectum seems to control convulsive states more readily than by way of oral administration.—H. W.

(PARATHYROIDS) The problem of spasmophilia (Ein Beitrag zum Spasmophilieproblem). Kleinschmidt (H.), Berl. klin. Wchnschr., 1918, **55**, 1017-1021.

Although this discussion fails to consider the possible role of the parathyroids in spasmophilia its conclusions are important as a point of view in their indirect endocrinological application. The author considers that the facialis phenomenon is of pathological significance at all ages of childhood, and indicates a congenital functional feebleness of the nervous system.—F. S. H.

(PINEAL) Epiglandol in dementia praecox. Becker (W. H.), Therapt. Halbmonat. (Berlin), 1920, **34**, 667-668.

Epiglandol is an extract prepared from the pineal. Fraenkel and Pilcz reported cases of dementia praecox with sexual irritability in whom a good effect was obtained after the injection of epiglandol. Becker tried it in 5 cases. In two of them no effect whatever was seen; in a third patient perhaps the inclination towards masturbation was decreased a little. The two other patients ceased masturbating after some injections. In none of the five patients could any other improvement be obtained.—J. K.

Contributions to the knowledge of the PINEAL gland in mammals (Bidrag til Kundskaben om corpus pineale hos pattedyrene). Krabbé (K. H.), Det kgl. Danske Videnskabernes Selskabs Biologiske Meddelelser (Copenhagen), 1920, **II, 2,** 1-111.

The author describes the embryological development and histological structure in a series of mammals: Two didelphys-embryos, talpa, erinaceus, sorex, vespertilio-embryos, vesperugo-embryos, spermophilus-embryos, guinea-pig, horse and pig-embryos, sheep, ox, dasypus, tatusia-embryo, cat, leopard, mustela, meles, halichoerus, phocaena (adult and embryos), several monkey-species (callithrix, macacus, cerecopithecus, cynocephalus, simia troglodytes). The comparative considerations showed that in most mammals the pineal gland consists of a rather uniform, non-follicular parenchyma. This consists in some mammals (phoca, rodentia, insectivora) of one species of cells (pineal cells) with a relatively large nucleus and a little protoplasm without distinct limits. In most mammals there is further a lot of glia-cells between the pineal cells. In the ungulates the glia-cells are predominating, more scarce in monkeys and carnivores. In higher monkeys and in man there are numerous nerve-cells in the parenchyma between the pineal-cells. The organ shows ordinarily a considerable vascularisation especially in halichoerus. Calcifications are found in man, in chimpanzee and the ox. Mast-cells are found in several mammals.

In dasypus the pineal gland is completely absent; in whales it is very rudimentary. The author describes further the different types of evolution in the fetal life. Concerning the function he concludes that the pineal gland evidently has a function in most mammals except the whales, edentates and perhaps the sirenia. The glandular structure, the amitoses, the high vascularisation point to a glandular function, but it must be taken into consideration more than it ordinarily is done, that this function might have a relation to the metabolism of the brain and the cerebrospinal fluid. The varying structure of the pineal gland, for instance the abundant development of nerve-cells in man and of glia-cells in ungulates could, indicates that the function is somewhat varying in the different mammals. The paper is illustrated with 71 figures.—Author's Abst.

The antidiuretic effect of PITUITARY extract in DIABETES INSIPIDUS. Davidson (M.), Lancet (Lond.), 1920, (ii), 401.

The patient, aged 35, complained of great thirst and polyuria, passing on the average over 300 oz. of urine per day. The urine was pale, acid in reaction, of low specific gravity (1000) and contained no sugar or albumen. A skiagram showed no abnormality of the sella turcica; his visual fields were not diminished nor was the fundus oculi abnormal. The patient was treated with daily injec-

tons of 1 cc. of pituitrin for 8 days and the quantity of urine was materially reduced and the specific gravity raised. Pituitrin given by mouth was without effect. When discharged, however, the polyuria still continued.—L. G. K.

Influence of PITUITARY extracts on the absorption of water from the small intestine. Rees (M. H.), Am. J. Physiol. (Balt.), 1920, **53**, 43-48.

The main object was to explain the antidiuretic action of pituitary extracts. The author has previously suggested that the antidiuretic effect may be due to interference with intestinal absorption of water (see Endocrin 1918, **2**, 188) and the present observations are concerned with this phase of the problem. The usual technique of cannulated loops was employed. The conclusion is, that while subcutaneous injections of pituitrin bring about delay in the absorption of water from the intestine, it is not sufficient to entirely account for the delayed excretion from the kidney. There is some constriction of the intestinal vessels, but not enough to cause variations in general blood pressure.—T. C. B.

Glycosuria during PREGNANCY. Cron (R. S.), J. Mich. M. Sc. (Grand Rapids), 1920, **19**, 399-404.

A positive reaction with Fehling's solution during pregnancy does not necessarily indicate diabetes mellitus, but usually lactosuria or alimentary glycosuria and rarely renal diabetes. Lactosuria may be looked upon as physiological during pregnancy for the reason that from 30 to 50 per cent of such females are less tolerant to glucose than non-pregnant females, although they show no hyperglycemia and are not true diabetics. Pregnancy may occur in diabetes or diabetes become manifest during pregnancy.—H. W.

(PROSTATE; GONADS) New facts on the pathology and surgery of the prostate with remarks on Steinach's experiments (Neueres aus Pathologie und Chirurgie der Prostata, zugleich Bemerkungen zur Steinachschen Verjüngungsmethode). Fischer (A. W.), Therap. Halbmonat. (Berlin), 1920, **34**, 658-661.

Prostatectomy means the removal of the submucous hypertrophical glands. Patients often become younger after the operation because they are rid of their urinary complaints. If a "catheter á dernieure" is the left in the bladder the same effect is seen. The cutting of the vas deferens produces a diminished growth of the submucous glands of th prostate. The publications of Steinach and Lichtenstein are not quite clear, since in none of the cases it is told whether the patients had urinary complaints or not. Only one case proves something. In this case fo Lichtenstein prostatectomy had not effect whatever. Ten weeks after the operation the vasa defer-

entia were ligated with success, as far as the senile symptoms were concerned.—J. K.

(PROSTATE; MAMMAE) Remarks on the article of Kondoleon: "Enlargement of the mamma after prostatectomy" (Bemerkungen zu der Arbeit Kondoleon's: Vergrösserung der Brustdrüse nach Prostatektomie). Zuckerkandl (O.), Zentralbl. f. Chir. (Leipzig), 1920, **47**, 1513-1514.

Kondoleon published in No. 36 of the same journal an article in which he maintained that he had observed two men in whom an enlargement of the breasts had occurred after prostatectomy. He concluded that the prostate has an internal secretion, the loss of which produced growth of the breasts. Zuckerkandl, however, makes the following criticisms: 1. Nothing is said of the histological processes in the enlarged breast. 2. What surgeons call prostatectomy has in reality nothing to do with it, but is only a removal of the hypertrophical submucous glands, while the prostate itself remains in the body. It is concluded then that Kondoleon's cases prove nothing. —J. K.

(SEX) Comparative anatomy of the genito-urinary organs of the lower animals. Tucker (H.), N. York M. J., 1920, **112**, 525-530.

General review of the primary and secondary sex characters in the lower animals. Nothing new.—H. W.

SEXUAL disturbances in wounded soldiers (Perturbamenti della sessualita' dei feriti di guerra. Desogus, Riforma Med. (Napoli), 1920, **36**, 583-585.

In 90 per cent of cases with cerebral lesions sexual alterations occurred, hardly ever in cases of peripheral nerve lesions and only when algias or traumatic neuroses followed the lesion. The localization of the cerebral lesion is immaterial. Desogus does not accept the endocrine theory as causative, since in experiments on adult animals not even with the removal of the **thyroid** could such a severe syndrome be obtained. The perturbations are laid to dynamic disturbance of the cerebral genetic centers.—G. V.

(SPLEEN) Splenectomy, with report of two cases. Miller (G. T.), N. York M. J., 1920, **112**, 304.

Good review of the relation of the spleen to disease.—H. W.

SPLEEN and carbohydrate metabolism (Milz und Kohlenhydratstoffwechsel). Togawa (T.), Biochem. Ztschr. (Berlin), 1920, **109**, 1-17.

Using many rabbits, frogs and guinea-pigs as experimental animals, Togawa found that after removal of the spleen the fasting

animals contained more glycogen than did the similarly treated unoperated controls although the blood sugar was the same both before and after operation. Extract of the spleen causes a decrease in the liver glycogen, and a slight hyperglucemia but no glucosuria. The injection of spleen extract tends to increase the adrenine hyperglucemia, but when the spleen is extirpated no disturbance of the adrenine hyperglucemia is produced. When fructose is injected intravenously into animals without spleens the resultant hyperglucemia is of a higher degree and lasts longer than in normal controls. When adrenine or strychnine is injected into such controls the loss of glycogen from the liver is greater than in animals from which the spleen has been removed when similarly treated. No changes were observed in the blood sugar concentration of normal animals when they were fed with desiccated spleen. It is concluded from these observations that the spleen plays a role in carbohydrate metabolism which warrants its placement with the other endocrine glands as a factor in the general system.—F. S. H.

(TESTES) Three clinical observations of primitive hypogenitalism under the type of eunuchoid feminism, gerodermia or genital dystrophic senilism of Rumme and Ferranni and telemorphism or regressive feminism (Tres observaciones clinicas de hipogenitalismo primitivo bajo el tipo de feminilismo eunuchoide, geroderma o senilismo genito-distrofico de Rummo y Ferranni y de telimorfismo o feminilismo regresivo). Castex (M. R.) & Waldorp (C. P.), Rev. de la Asoc. med. argent. (Buenos Aires), 1920, **33**, 458-476.

Three typical cases discussed from the point of view of endocrine participation. They are attributed by the authors to hereditary syphilis.—B. A. H.

The effects of ligating the TESTES of hen-feathered cocks. Morgan (T.), Biol. Bull. (Phila.), 1920, **39**, 248-256.

Ligation of the testes in adult cocks of hen-feathered races results in the atrophy of the glands. Cock-feathering follows this operation.—W. J. A.

(TESTES) Orchitis in mumps. Wesselhoeft (C.), Boston M. & S. J., 1920, **183**, 425-430; 458-460; 491-504; 520-524.

The author, after citing many interesting references concerning the relation of mumps to the sex glands, adopts the following tentative theory to explain the connection of mumps with orchitis: (1) Chemotaxis of groups of tissue cells in various parts of the body for certain poisons (Abderhalden) and, (2) Selective affinities of certain strains of a given organism for certain tissues of the body (Rosenow). The testes alone are not involved in mumps but also

the **ovaries**, and Bartholini's glands; mastitis, adenitis, dachryocystitis, and **pancreatitis** are among the complications of the disease. Involvement of the **prostate** gland (atrophy) is far more apt, than orchitis, to bring about sterility for the reason that an insufficient prostatic fluid during emission greatly decreases the chances of fertilization. Orchitis as a complication of mumps is confined to the age of puberty and adolescence. Orchitis occurred as a complication of mumps 1,468 times in a series of 8,153 cases or in 18 per cent.

Mumps may be manifest solely in the testicle. Atrophy of the testicle following orchitis occurs within from 4 to 6 weeks after the onset and is observed in 54 per cent of the cases. Orchitis and atrophy of the gland may not be associated with disturbances of any kind, however, disagreeable sensations, intense neuralgic pain, decreased sexual appetite (temporary), with diminished ability to perform coitus, or active sterility may result as sequences of orchitis. "Feminism" rarely develops and when present indicates a previous double orchitis. Mumps are so rare before the period of puberty that no eunuch has been described as the result of this disease. The author calls attention to the fact that mumps are rarely the cause of permanent sterility and that atrophy of the testicle does not usually involve all of the spermatic tissues present in the gland. The article closes with a consideration of the prophylaxis and treatment of mumps and an appendix of 77 references.—H. W.

(TETANY) Some rare consequences of influenza (Seltene Folgeerscheinungen der Influenza). Berger, Wien. klin. Wchnschr., 1920, **33**, 742.

A demonstration of a patient with tetany and ptyalism following influenza. These symptoms began three weeks after the fever had disappeared. At the same time the patient complained of pyrosis without hypersecretion of the stomach, dermographia, or urticaria-like symptoms of the skin. These symptoms are said to be proof of vagotonia. The patient had had a light post-operative tetany for the preceding seven years and which was increased by the influenza; but became latent again after subsidence of the fever.—J. K.

Contribution to the anatomical and pathological study of the THYMUS in infants (Contributo allo studio anatomico e pathologico del timo nella prima eta'). Canelli (Adolpfo F.), La Ped. (Napoli), 1920, **28**, 753-764.

Canelli reports the result of a study of the post-mortem findings in 115 cases and concludes that in order to observe the thymus at its best we must be able to see its relations to the jugular notch, therefore the sternum must not be removed at first. Topographically we may make three classifications of thymus, i.e., Thoracic, Cervico-

thoracic, and Cervical. This last can be considered ectopic. As regards the number of lobes, in order of frequency, we have the bilobatus, unilobatus, trilobatus and scutaneous types. The greatest part of hypertrophic thymus' belong to the bilobate form. The color of the thymus is related to the general conditions of nutrition, to local diseases, to general diseases and to the post-mortem condition. The relative weight (fresh gland) varies within very wide limits, as it is, especially in the first four years of life, dependent on the course and the nature of the disease. The average water content seems to be in an inverse ratio to age.—G V

(THYROID) Radium in goiter. Aikins (W. H. B.), Am. J. Roentgenol. (Detroit), **7**, 404-411.

After presenting the outstanding symptoms of toxic goitre the author reviews the theories of its etiology. The body of the paper, however, is devoted to a discussion of the treatment, based upon 12 years' experience. The author's technique of applying radium is given and a series of cases reported. It is his opinion that the effect of radium in toxic goitre has been in some respects similar to x-rays but that the former has many advantages. Some of these are exactness of dosage, far greater penetration and the absence of a noisy exciting apparatus.—J. F.

(THYROID) Diagnosis of myxedema. Anders (J. M.), Am. J. M. Sc. (Phila.), 1920, **160**, 801-808.

Many cases of myxedema go unrecognized even by experienced clinicians. Of 55 cases collected from the American and Canadian literature 74 per cent had failed of diagnosis by one or more physicians. The most characteristic signs of myxedema are firm, inelastic thickening of the skin and subcutaneous tissue which does not pit on pressure and mask-like immobile features. The mucous membranes are often infiltrated and the teeth may become loose. The tongue, lips and nose are thick and the voice has a peculiarly monotonous character, with frequent curious nasal explosions. Cerebration is characteristically slow, though memory may be good. Scantiness of hair is common. Albuminuria is frequently found and occasionally casts in the urine, hence the condition is often mistaken for nephritis, little as the two conditions fundamentally resemble each other. Rudimentary myxedema is frequently associated with other endocrinopathies, especially acromegaly. In such cases the addition of thyroid to other appropriate treatment may give brilliant results. Anders believes that exophthalmic goitre and hypothyroidism are frequently co-existent. In cases of suspected myxedema, and especially when evidence of other endocrinopathies is found, the administration of thyroid material as a therapeutic test is often advisable. In view of their amenability to treatment, the recognition

of incomplete types of myxedema is important. As pointing to the correct diagnosis, subnormal temperature with chilly sensations, yellowish, firm, inelastic skin, depressed perspiration, general "bulkiness," with facial stolidity, irritability, and more or less circumscribed thickening of the skin and mucous membranes are especially significant. In illustration of the chief points in the article a case is reported.—R. G. H.

THYROID dysfunctioning resulting in nanism and infantilism (Presentation d'un cas de nanisme et infantilisme d'origine dysthyroidienne). Armand-Delille (P. F.), Bull. et mém. Soc. méd. d. hôp. d. Par., 1920, **44**, 1392-1395.

The patient was a man of 22 years presenting the appearance of a boy of 12. The stature was 1 m. 32 and the weight 36 kilos. The external genitalia were infantile but normally formed. No testicular exctopy was present. There was absolutely no development of axillary, or pubic hair. Epiphyseal union had not occurred. Intelligence was about normal. The thyroid was not palpable. Thyroid medication was begun but no report of the result is given.—F. S. H.

Anatomical changes in and insufficiency of the THYROID (Anatomische Veränderungen der Schilddrüse und Schilddrüseninsuffizienz). Berlinger, München. med. Wchnschr., 1920, **67**, 1334.

Data reported elsewhere.—J. K.

(THYROID) Co-relation of results of treatment by surgical and x-ray methods. Bingham (G. H.) & Richards (G. E.), Canad. M. Ass. J. (Toronto), 1920, **10**, 988-995.

It is pointed out that since "immature cells and cells in an active state of division are more sensitive to x-rays than are cells which have acquired their fixed physiological character," the effect of x-rays upon the thyroid should take place in the following order: The hyperplasias should be influenced most, the adenomatous type next, and the cystic type should practically not respond at all. This is borne out by the authors' experience. They adopt Judd's classification of simple colloid, adenomatous and toxic goitres. Of the simple colloid goitres 90 per cent were completely cured by x-ray treatment. The adenomatous type was found to respond very poorly, and surgical treatment is advised for them. Of 300 toxic cases 50.3 per cent were completely cured, 11.3 per cent were improved and 5.3 per cent showed no improvement. The remainder were not classified. The order of disappearance of the various symptoms is as follows: Nervousness and irritability, tremor, tachycardia, loss in weight, goitre, exophthalmos. The length of time required for each case is from 6 to 8 weeks. The cases which

are not definitely cured but are improved, are made thereby much safer surgical risks. The advantages of the method are the ease with which it may be carried out, its safety to life, its painless nature, and freedom from shock. Its disadvantages are the length of time required and the possible production of fibrosis of the capsule.—L. G. K.

(THYROID) The cardinal diagnostic manifestations in exophthalmic goiter with report of cases. Butler (E. E.), Kentucky M. J. (Bowling Green), 1920, **18**, 367-369.

A general discussion of the cardinal symptoms of exophthalmic goiter and the presentation of 3 cases; nothing new.—H. W.

(THYROID) Contributions to the Biochemistry of Iodine. III. The comparative effects of thyroid and iodide feeding on growth in white rats and in rabbits. Cameron (A. T.) & Carmichael (J.), J. Biol. chem. (Baltimore), 1920, **45**, 69-100.

This paper gives a semi-critical review of the studies made of the effects of feeding thyroid and iodides to various animals. The authors report a similar study on 40 male and 16 female white rats. Of these, 31 males and 16 females were from 9 litters; and 7 controlled experiments were carried out with thyroid and 4 with sodium iodide. The initial age of feeding varied from 40 to 60 days and the periods of observation varied from 18 to 72 days. The remaining 10 animals were of different ages and from different litters and were used in the specific experiment to induce tetany by feeding large doses of thyroid. The diet used was bread and milk throughout with one exception. Three thyroid preparations were studied. In one experiment 5 rabbits from one litter were used. Extensive tabulations are made and protocols given. The effects of the feedings on the body growth, weight and length, and on the size of the liver, kidneys, heart, spleen, lungs, testes, adrenals and thyroid are recorded. The results indicate to the authors that continued small doses of desiccated thyroid gland fed to young white rats produce (a) a definite and invariable decrease in growth rate; (b) hypertrophy of the organs concerned with increased metabolism-heart, liver, kidneys, adrenals, etc.; (c) disappearance of fat. They also claim that the decrease in rate of growth is proportional to (a) the amount of thyroid fed and (b) the iodine content of the thyroid fed. The hypertrophy varies with the dose and length of application of dose, and appears to be proportional to the iodine content of the dose. When sodium iodide is fed in amounts varying from quantities equal in iodine content to the thyroid doses to amounts 100 times as great, no effect on growth rate or hypertrophic changes are produced. Both the thyroid and the iodide feeding increase the colloid in the thyroid and thyroid feeding inhibits the growth rate of the thyroid. Iodide does not pro-

duce this effect. The suggestion is made that since of numerous tissues tested only thyroid produces this effect, thyroid feeding can be used as a discriminatory test for preparations alleged to contain the essential thyroid secretion. (It is the opinion of the abstractor that the number of experiments described are quite insufficient for the determination of all the points discussed, particularly since the authors themselve state and their figures show that wide variations occurred.)—F. S. H.

(THYROID) Acute, Febrile, Epidemic Myxedema with Tracheal Stenosis (Mixedema acuto febbrile epidemico con stenosi tracheale). Citelli (S.), Riv. Crit. di Clin. Med. (Firenze), 1920, **21**, 262.

Citelli reports an epidemic of febrile acute myxedema characterized by swelling of head, neck and thorax, often complicated with tracheal stenosis. The patients all recovered within a few weeks.—G. V.

THYROID gland of the tuberculous (Le corps thyroide des tuberculeux). Coulaud. Bull. et mém. Soc. Méd. d. hôp. d. Par., 1920, **44**, 1551-1555.

Coulaud reports the results of an examination of 120 thyroid glands obtained from as many cases of pulmonary tuberculosis. No record was kept of the size of the glands examined. Of the 120 studied, three exhibited tuberculosis of the thyroid itself. There was one parenchymatous goiter and two of the cystic type. Frequently microscopic evidence of a cystic tendency coinciding with diffuse sclerosis was obtained. Twelve cases showed thyroids apparently entirely normal in function. Some fourteen of the glands examined gave no definite evidence of a functional diminution, although a tendency to follicular hyperplasia was present. The residual cases showed large areas of peri-vascular sclerosis embedded in a glandular parenchyma poor in connective tissue and apparently normal, or else abundant connective tissue around the vessels and prolongations into the intervesicular spaces.

Coulaud concludes from this extensive study that the thyroid gland functions well in the tuberculous, perhaps a bit too much, in spite of the sclerotic lesions that are present. He intimates that possibly the sclerosis is a sequel of the intensive functioning of the gland.—F. S. H.

(THYROID) The concentration of the serum and the viscosity of the blood in myxedema and the effect of thyreoidin on them (Serumkonzentration und Viskosität des Blutes beim Myxödem und ihre Beeinflussung durch Thyreoidin.) Deutsch (G.), Deutsches Arch. f. klin. Med. (Leipzig), 1920, **134**, 342-351.

The viscosity of the total blood remains normal in myxedema, while the viscosity of the serum is increased. Hence it is probable that the quantity of protein is high. This is confirmed when the serum is examined with the refractometer. The refractory index is high in myxedema, especially in the more serious cases. In some cases of hypofunction of the thyroid without myxedema the same is observed. The administration of thyroid was in all cases of myxedema and in most cases of hypothyroidism followed by a decrease of the protein-content and of the viscosity of the blood. Only in one case of myxedema (produced by x-ray treatment of Graves' disease) and in a few caes of hypothyroidism this effect was not observed. In these cases the administration of thyroid had likewise no influence on the other symptoms.—J. K.

(THYROID) The Diagnostic Value of the Estimations of the Basal Metabolic Rate. Else (J. E.), Northwest Med. (Seattle), 1920, **19**, 171-175.

The author devotes about half of his article to a compact historical summary of the development of basal metabolism from the purely scientific physiological investigations of Liebig, Voit, Lavoisier, Pettenkoffer and Rubner, and to the practical application of this knowledge mostly in America by Atwater and Rosa, Gephart and Du Bois, and Benedict. Else then records briefly the observations of Friedrich Müller in cases of thyrotoxicosis, the fundamental work of Magnus-Levy in first demonstrating and calculating the lowered metabolism in hypothyroidism and the opposite condition in hyperthyroidism by indirect calorinetry. Details are then given of the actual operation with a Benedict apparatus and the method of calculating the basal metabolic rate. Else does not determine the respiratory quotient, but uses 0.82 as recommended by Benedict, Emmer, Roth and Smith. Three illustrative cases are presented, one of hyperthyroidism with rate of 72 per cent above normal, one of hypothyroidism, rate 28 per cent below; and a myxosarcoma of the thyroid with normal rate of 5 per cent above theoretical normal. Twenty-four references to the literature are appended.

—H. L.

(THYROID) The technic of goiter operation (Zur Technik der Kropfoperation). Enderlen (E.) & Hotz (G.), Zentralbl. f. Chir. (Leipzig), 1920, **47**, 1365-1366.

Ligation of all four arteries of the thyroid in operation for goiter has been recommended, but Madlener, who has performed this operation, observed 24 days later a postoperative tetany, ending fatally in 6 days. According to the authors this cannot be due to the operation, since they ligated the four arteries in thousands of cases without ever observing tetany. If Madlener would be right transplantation of endocrine organs would never be possible. Mad-

lener observed suppuration in his case after the operation. It is very probable that this suppuration caused necrosis of the parathyroids.—J. K.

(THYROID) Colorimetric studies of tryptophan. II. (Colorimetrische Untersuchungen über das Tryptophan. II. etc.). Fürth (Otto) & Lieben (Fritz), Biochem. Ztschr. (Berlin), 1920, **109**, 124-152.

The thyroid gland of man is relatively rich in tryptophan by the new method of determining this substance described by the authors.—F. S. H.

(THYROID) Diagnosis and treatment of hyperthyroidism. Fussell (M. H.), N. York M. J., 1920, **112**, 205-212.

Conditions of hyperthyroidism must be differentiated from cases of neuresthenia. In the neuresthenic muscular tremors are intermittent, the mental character is introspective, there is no flushing of the skin, the heart slows while recumbent, there is a loss of appetite, the metabolic rate is not increased, the Goetsch test is negative, sugar tolerance is normal and there is no response to thyroid preparations. On the other hand the hyperthyroid patient presents continuous muscular tremors, flushing of the skin, an alert and apprehensive mental character, dilation of the heart, an increased appetite, an increased metabolic rate, a positive Goetsch test and active responses to thyroid medication. The treatment of hyperthyroid cases should consist of rest but where this is not possible the gland should be operated upon. If the individual is toxic, rest, ligation of thyroid arteries and the x-ray should be tried before surgery is resorted to.—H. W.

(THYROID) Cure of tuberculous goiter (Contributo alla cura della struma tubercolare). Giacinto (G.), Policlin. (Roma), 1918, **25**, sez. chir., 225-230.

Giacinto reports the case of a man, 42 years old, who for eight months had noticed that the right lobe of the thyroid gland was enlarging. Irregular neuralgic pains were also felt in the tumor, irradiating downward and outward or upward. These pains were variable, appearing usually in the evening, and were not modified by the ordinary sedatives. The temperature rose slightly toward evening. The hard tumor was tender, with irregular surface, and immovable except for slight movement during swallowing. There was slight emotional tachycardia, but no signs of exophthalmic goiter. The urine was normal. The weight had dropped over 15 pounds in two months. The diagnosis wavered between malignant goiter and woody thyroiditis, but an exploratory incision showed the capsule much thickened and bound down to adjacent tissues. A wedge was excised, 5 cm. long by 3 cm. wide; the inner

end seemed to be normal tissue, but a cheesy tubercle was apparent above. No tubercle bacilli could be discovered. Treatment by daily injection of alternating iodin and arsenic was successful.
—F. S. H.

(THYROID) The Heart in Graves' disease. Goodall (J. S.), Practitioner (Lond.), 1920, **105**, 37-46.

The condition of the heart is of immense importance in Graves' disease in deciding prognosis and in determining the type of treatment. The extent of cardiac pathology depends upon (a) the duration of the disease, (b) the intensity of the intoxication, (c) the pre-existing state of the heart. The systolic blood pressure, according to Goodall, is usually 10 to 20 per cent below normal, the diastolic is about normal, the pulse presure is low. Operation on the thyroid raises the blood pressure, sometimes enormously and acutely and the author believes over-action of the adrenals to be the cause of sudden death after thyroid operation. In the average case, the blood pressure is raised at first for a short period then falls below normal for a longer time, which is the "safe operation stage," then rises again, either due to adrenal activity or cardiac hypertrophy. The low pressure stage is recommended for operative intervention because of (1) only slight myocardial exhaustion; (2) less risk of postoperative acute rise with sudden death from ventricular fibillation; (3) little risk of hemorrhage. Goodall points out that his views are not in agreement with Kocher. Several types of electrocardiographic tracings are included. The tachycardia of Graves' disease is shown to be supra-ventricular, auricular in origin. As myocardial exhaustion increases, atonia sets in and gradual dilation follows. True angina in Graves' disease is said to be exceedingly rare. The electrocardiogram in moderately advanced cases will show left ventricular proponderance and lengthening of the P.R. interval showing impaired conductivity of the Bundle of His. Finally auricular fibrillation appears. Turning to treatment, Goodall apparently places no faith in medical remedies. Even x-ray is not highly recommended. Attention is called to the danger of burns, the inability to gauge the dose accurately and the rendering of operation more difficult. The author favors operation and suggests that the amount removed should depend on the severity of the symptoms. Preliminary ligation is advised in selected cases. (Many authors would disagree with Goodall's ideas about blood pressure and therapy).—H. L.

(THYROID) A contribution on blood pressure in Graves' disease. Goodall (J. S.) & Rogers (L.), Brit. M. J. (Lond.), 1920, (ii), 588-590.

The authors quote a series of 20 cases of exophthalmic goitre, 10 in women and 10 in men, to show that the systolic blood pres-

sure is generally considerably below that expected for normal individuals of the same age. The diastolic pressure is very little affected. The blood pressure is relatively lower in the women than in the men, but the occurrence of pre-existing arteriosclerosis or ventricular hypertrophy is advanced as an explanation of the higher blood pressure seen in most of the males. The authors believe that the blood pressure in Graves' disease passes through three stages: (1) a preliminary stage of hypertension associated with the onset of the disease, and of brief duration; (2) a stage of hypotension, which is relatively long, lasting for months or years; (3) a stage of secondary hypertension which appears to be associated with "a reduction of thyroid superactivity, with consequent relative increase in that of the suprarenal" and "some secondary change in the cardio-vascula system, such as cardiac hypertrophy." The second stage is regarded as a safe operative condition. Often a marked post-operative rise in blood pressure occurs. This is not infrequently associated with cardiac acceleration and irregularity of the pulse due to auricular fibrillation. In extreme cases ventricular fibrillation may cause death. "A low systolic pressure in Graves' disease, other factors being equal, indicates from an operative point of view: (i) little myocardial exhaustion, (ii) a small post-operative rise in blood pressure and consequently little liability to post-operative cardiac failure, (iii) less hemorrhage."

—L. G. K.

(THYROID) Ueber sporadischen Kretinismus. Guleke, Berl. klin. Wchnschr., 1920, **57**, 861.

Data published elsewhere. (See Endocrinology, **4**, 700).—J. K.

(THYROID) Diffuse colloid goitre (Die diffuse Kolloidstruma). Hellwig (A.), Mitt. a. d. Grenzgeb. d. Med. u. Chir. (Jena), 1920, **32**, 508-540.

A very detailed report of histological studies and review of the literature on the subject. The author considers the "struma diffusa colloides" as a thyroid with an increased function due to infection with the hypothetical "Kropftoxin." These patients show an increased irritability of the involuntary nervous system, and their endocrine system is hardly equilibrated. Administration of iodine, psychical or physical over-stimulation may produce Graves' disease in these individuals.—J. K.

(THYROID) Diagnosis of hyperthyroidism. Johnson, (C. H.), J. Mich. M. Sc. (Grand Rapids), 1920, **19**, 456-459.

A negative **adrenin** test excludes **hyperthyroidism** while a definite positive test means hyperthyroidism in all but a small percentage of the cases. This test is always positive in true cases of hyperthyroidism.—H. W.

The postulated antagonism between THYROID and SPLEEN (Über den angeblichen Antagonismus von Schilddrüse und Milz). Klinger (R.), Biochem. Ztschr. (Berl.), 1918, **92**, 376-384.

This paper is a report of a study of the oxygen consumption, thrombin content of the serum and bone-marrow of thyroidectomized or splenectomized rats and cats. The results of the study afford no confirmation of the idea of the existence of an antagonism between the spleen and the thyroid.—F. S. H.

(THYROID) Remarks on goiter (Based on 190 thyroid operations by the author). Lahey (F. H.), Vermont Med. (Rutland), 1918, **3**, 30-33.

A brief review with no novel data.—F. S. H.

THYROID injection in cachexia strumipriva (Injecto de tiroides en una caquexia estrumipriva.) Lenzi (L.), Semana méd. (Buenos Aires), 1918, **25**, pt. 2, 61-62.

A brief statement that the injection of thyroid extract in a case of cachexia strumipriva ameliorated the distressing symptoms. —F. S. H.

THYROID instability and neuro-arthritis with multiple swellings (Neuroarthritisme a fluxions multiples par instabilité thyroidienne). Léopold-Levi Presse méd. (Paris), 1918, **26**, 191-192.

A case report of a neuropathic case bordering on neurasthenia accompanied by arthritis. The thyroid gland gave evidence of frequent congestive attacks by its repeated swelling and subsequent reduction in size. Other tissues and parts of the body exhibited this alternating enlargement and regression. The case was diagnosed as a neuro-arthritis predominately angio-neurotic. The evidences of hyperthyroidism were plentiful and confirmed the hypothesis of a thyroid instability regulable by thyroid administration. The author considers that the angio-neurotic condition is the basis of the congestive disturbance of the thyroid leading to the appearance of hyperthyroidism.—F. S. H.

THYROID gland. Lim (R. K. S.), Sci. Progress (London), 1920, **15**, 243-249.

Hyperthyroidism, hypothyroidism, the function of the thyroid in the lower vertebrates, the nature of the thyroid secretion, and the function of the secretion of the parathyroids are discussed. The conclusion is drawn that "the function of the thyroid varies according to age. In the young it hastens development, in the adult it maintains the working of the body processes at a normal rate, and in the aged it probably ceases to function."—Chem. Abst., **15**, 257.

(THYROID) Flatulant dyspepsia of Basedowians (La dyspepsie flatulente des basedowiens). Loeper (M.), Prog. méd. (Paris), 1918, 3.s., **33,** 345-347.

Out of 40 cases of Basedow's disease, Loeper reports four with diarrhea and 13 with dyspepsia. The flatulent dyspepsia is attributed, not to thyroid hypersecretion but to compression. Nevertheless there are other dyspepsias that may be considered as taking their origin from the toxic thyroid.—F. S. H.

THYROID glands—metastasizing effects. McLean (A.), J. Mich. M. Sc. (Grand Rapids), 1920, **19,** 558-560.

A general discussion of thyroid metastases and their relation to malignant growths.—H. W.

(THYROID) Case of early myxedema. Mahon (F. F.), J. Roy. Nav. M. Serv. (Lond.), 1917, **3,** 481-482.

A brief report of a patient showing the early signs of myxedema. The disease was aborted by treatment with thyroid extract and potassium iodide. One 5 grain B. & W. thyroid tablet was taken daily; when less was ingested a relapse occurred.
—F. S. H.

(THYROID) A case of myxoedema. Mathers (A. T.), Canad. M. Ass. J. (Toronto), 1920, **10,** 859-862.

The patient was a married woman, aged 32, anemic and somewhat emaciated in appearance. There was a yellowish tinge to the skin which was dry. The hair was dry and of a very fine texture. The nails were brittle. In the region of the eyes and across the bridge of the nose some oedema was present. Physical and mental processes were slower than normal. Mental examination showed that hallucinations were very evident and that delusions of persecution were prominent. A gastro-intestinal x-ray series revealed "a remarkable degree of atony and stasis throughout the whole tract." The case was diagnosed as myxoedema and the patient was placed on thyroid extract—two grains three times a day. The dose was gradually increased, and in a short time the mental symptoms entirely disappeared, and a second x-ray series showed that the gastro-intestinal stasis and atony had completely vanished. The contention that the secretion of the thyroid has an activating influence on the abdominal vagus would seem to be borne out by the results in this case.—L. G. K.

(THYROID) Goitre. Matthews (A. A.), Northwest Med. (Seattle), 1920, **19,** 183-185.

Matthews reports 75 consecutive goitre operations with three deaths. He warns of the frequent intolerance to surgery in the

toxic goitre patient and the importance of patience and conservatism. Plummer's classification of goitre is adhered to. The cautious use of iodides in physiologic-non-surgical goitre is recommended. Matthews believes that endemic goitre is dependent on water from so-called goitrous wells that have passed through certain geologic strata. Bircher's important experiments are referred to. The theory of McCarrison that goitre is due to toxic substances of infectious origin, chiefly from the colon, is alluded to, and the interesting cures or improvement in cases of exophthalmic goitre obtained by him and Lane in short circuiting the large bowel. Matthews considers the non-hyperplastic toxic goitre more dangerous than the exophthalmic goitre. The author seems to lack confidence in the permanency of cure by medical treatment in toxic goitre, but in advocating surgery points out that success in thyroid surgery depends on wise judgment, as to when to operate and how much to operate.—H. L.

(THYROID) Pathology of the heart in myxedema (Zur Klinik des Myxödemherzens). Meissner (R.), München. med. Wchnschr., 1920, **67**, 1316-1317.

A report of three cases.

1. A man of 56 suffered since 12 years old from classical myxedema. The heart was enormously dilated on the right and on the left. The heart sounds were normal. The pulse rate was 50-52. The x-ray picture showed an enormous heart and an enlarged aorta. The volume of the heart became normal again after treatment with thyroid.

2. A woman (age not given) with hypothyroidism. The heart was dilated on the left side. The second aortal sound was accentuated. Pulse 58. The face and tongue were swollen. The urine contained leucocytes, erythrocytes and albumen, but no casts. Edema of the ankles was present. Blood pressure 180. The diagnosis as between myxedema and nephritis was very difficult. By thyroid treatment the urine became normal; the blood pressure sank temporarily, the pulse rate was raised but the heart remained unchanged. Perhaps the dilation of the heart was due to another cause (nephritis) as the other symptoms of hypothyroidism.

3. A woman of 39 became acutely ill with swelling of the face and tongue and loss of hair. Pulse rate of 54. The heart was normal. She was cured by thyroidin, though the heart did not undergo any change by this treatment. Probably the disease was too acute to produce changes in the heart.—J. K.

(THYROID, PARATHYROID) The effects of thyreo-parathyroidectomy in the guinea pig. (Sur les effets de la thyreo-parathyreodectomie chez le cobaye). Mira (M. F. de), J. de Physiol. et de Path. Gén. (Paris), 1920, **18**, 976-980.

The total removal of the thyroids and parathyroids in 12 animals was found to cause death in from 2 to 57 days. Apathy and slowness of movement and generally fibrillary twitching of the muscles occurred. Tetanic attacks preceded death. Convulsive seizures were absent in some cases of prolonged survival. Most of the cases were characterized by loss of weight. The results were independent of the ages of the animals.—L. G. K.

THYROID treatment of edema (Oedembehandlung mit Schilddrüsenpraparaten). Molnar (B.), Wien. klin. Wchnschr., 1920, **33**, 1111-1114.

The author employed thyroid therapy in 20 cases of edema. He began with 1 gram of dry gland daily; in one case he even gave 3½ grams daily without complications. In four cases of nephrosis, a good result was obtained in two. In five cases of Bright's disease no result was seen. No success was observed in five patients with cardiac myo-degeneration. In another case, however, the result of the thyroid treatment was indirect. First, digitalis and caffein had no effect; then thyroid was tried during 16 days without success. After this digitalis was once more tried with a most brilliant result. A patient with lymphogranulomatosis and acromegaly, with cardiac insufficiency, edema, ascites, hydrothorax when treated with thyroid, became markedly diuretic with loss of weight. In this case it is not quite sure that the polyuria was due to the treatment, since the patient had a tumor of the hypophysis, to which the polyuria might have been due.—J. K.

(THYROID) The medical aspects of Graves' disease. Morsman (C. F.), Northwest Med. (Seattle), 1920, **19**, 178-182.

Morsman prefers the terms Graves' disease to exophthalmic goitre because exopththalmus is frequently absent, and to hyperthyroidism because other ductless glands are often involved. He mentions the preponderance of Graves' disease in females and the probable relations with the gonads as evidenced by physiologic hyperthyroidism in adolescence and pregnancy. The author does not agree with Leonard Williams that Graves' disease is the adult form of mongolism. The alimentary hyperglycemia of Graves' disease is discussed together with the technic of obtaining the blood sugar curve. In discussing treatment Morsman points out that treatment either by surgery, x-ray or radium of the thyroid gland is not sufficient because disturbances occur in other structures than the thyroid; dietetic and hygenic treatment must also be employed; closer relation between the trained internist surgeon and roentgenologist will serve the patient best. Various drugs and ductless gland products that have been tried in Graves' disease are briefly commented upon.—H. L.

(THYROID, ADRENIN) The differentiation of early tuberculosis and hyperthyroidism by means of the adrenalin test. Nicholson N. C.) & Goetsch (E.), Canad. M. Ass. J. (Toronto), 1919, **9**, 481-489.

There are many patients who symptomatically might be considered as suffering from either incipient tuberculosis or mild to moderate hyperthyroidism, or both. The authors use as a diagnostic aid in these conditions the constitutional hyper-sensitiveness to adrenin exhibited by all cases of hyperthyroidism, whether associated with tuberculosis or not. Tuberculosis uncomplicated by hyperthyroidism does not cause a positive reaction to adrenin. The test is carried out as follows: After a day of complete rest in bed two readings are taken at five minute intervals, of systolic and diastolic blood pressure, pulse rate, and respiration, and all signs and symptoms of hyperthyroidism are noted; 0.5 cc. of a 1:1000 adrenin solution is injected subcutaneously in the deltoid region. Records of pulse and blood pressure are then made every two and one-half minutes for ten minutes, then every five minutes up to one hour, then every ten minutes for half an hour or longer. In a positive reaction there is usually an early rise in blood pressure and pulse of from 10 to 50 points. In the course of half an hour there is a moderate fall, then a slight secondary rise, then a fall to normal in about 90 minutes. Along with these there is an exaggeration of the clinical picture of hyperthyroidism, especially the nervous manifestations such as tremor, apprehension, throbbing, asthenia, vasomotor changes. A majority of these signs and symptoms must be definitely brought out or increased before the test can be regarded as positive.—L. G. K.

(THYROID) Goiter. The indications for and the technic of the surgical treatment of goiter, illustrated by three cases. Ochsner (A. J.), Surg. Clin. Chicago (Phila.), 1917, **1**, 47-63.

The indications for surgical interference in goiter patients according to Ochsner are, the development of the growth to the point where evidences of toxemia are given, when it interferes with deglutition and respiration, and when it refuses to respond to medical treatment after a reasonable length of time. The inference is made that such operations should not be done during puberty. The three cases described are used to illustrate the preparatory and surgical technic employed. In order that as little anesthetic as possible be used, so that the danger from post-operative pneumonia be minimized, Ochsner gives ¼ grain of morphine and 1/100 grain of atropin hypodermically one-half hour before anesthesia, and when anesthesia is complete raises the head of the patient to an angle of 45 degree, thus producing cerebral anemia and making anesthetization during the operation unnecessary. Sufficient thyroid tissue is left behind in every instance to provide for about the

normal secretion. The after-treatment consists in proctoclysis with 500 cc. normal salt solution started every four hours. If the pulse tends to rise and excitement occurs a hypodermoclysis of 1000 cc. normal salt solution is given in the pectoral region. On leaving the hospital the patient is cautioned against excitement, the eating of meat, and the drinking of stimulants.—F. S. H.

(THYROID) The differential diagnosis of tuberculosis. Otis (E. A.), Boston M. & S. J., 1920, **183**, 695-702.

Hyperthyroidism is not infrequently seen in many persons who show early signs of tuberculosis, i. e., tachycardia, frequent sweating, lassitude, cough and evening temperature.—H. W.

(THYROID) Goitre and its medical treatment. Pearson (J. M.), Canad. M. Ass. J. (Toronto), 1920, **10**, 983-987.

In the treatment of those forms of goitre producing symptoms of hyperthyroidism the necessity for rest and correct feeding is emphasized. The rest must be such that the environment is as closely adapted as possible to the individual, and all channels of disturbance alike to physical and mental sides closed. An oversupply of assimilable food should be provided. Certain diets with a high iodine content seem to prevent the occurrence of goitre. The Japanese use seaweed as a food and they are practically immune to goitre. Seaweed contains a large quantity of iodine. Certain drugs are briefly mentioned since they are used to some extent in the treatment of goitre.—L. G. K.

Myxedema with complete THYROID aplasia (Ueber myxödem bei totaler Thyreoaplasia). Rössle. Berl klin. Wchnschr., 1920, **57**, 861.

A demonstration of the organs and the skeleton of a dwarf of 28 in whom thyroid tissue could not be found at autopsy. The patient died of cirrhosis of the liver with intestinal hemorrhages. There was an arteriosclerosis, and the ossification was defective. The skin showed all symptoms of myxedema. The uterus and **ovaries** had the shape of a full grown woman. There were no secondary sexual characteristics. No **parathyroids** were found on the right, but were present on the left side. The **hypophysis** was rather large (725 mg.) and contained two adenomas. No traces of thyroid was found in the tongue. The zona glomerulosa of the **adrenals** showed a marked sclerosis. The **thymus** was changed into fat. The **pineal, pancreas** and **spleen** were normal.—J. K.

(THYROID) Idiopathic Osteopsathyrosis (Osteopsatirosi idiopatica). Ruggieri (Elvino), La Ped. (Napoli), 1920, **28**, 953-974.

The article is a detailed report of a case of osteopsathyrosis in a girl 13 years old, who had to that age eleven fractures of long bones. When she recovered she could not even walk, if not held. On account of the disturbed calcium metabolism **adrenal** treatment was given for a month, but with little result. **Thymus** gland was then added to the adrenal and in seven weeks from her entrance she became able to walk by herself and her weight increased from 19 kilos to 23.5 kilos. The author believes that it was a question of prenatal endocrine disturbance.—G. V.

(THYROID) Toxic goiter in orientals. Russell (W. B.), Nat. Med. J. (Shanghai), 1920, **6**, 101-108.

After a brief review of papers dealing with the general subject of goiter in China the author describes in some detail five selected cases of toxic goiter which present no special feature not found in occidentals. He recommends the usual operative treatment if satisfactory improvement does not follow rest and improved by hygienic conditions. This article is of value in connection with the suggestions of Arthur Keith and others that the Chinese as a race present the phenomena of reduced thyroid secretion.—E. V. C.

(THYROID) The therapy of Flajani-Basedow's disease (Sulla terapia della malattia di Flajani-Basedow). Schiassi, Reforma med. (Napoli), 1920, **36**, 829.

Considerations on the article published by the Policlinico-Surgical section—in which Prof. Schiassi claims that 60 per cent of the cases are apt to recover. He considers the toxemia as also influencing the functions of the **ovaries** and **adrenals.** He claims good effects from belladonna, does not trust the x-rays on account of a possible danger to the **parathyroids,** repudiates cervical sympathectomy and advises the surgical intervention on the gland only when the medical treatment proves of no avail.—G. V.

Influence of an alcoholic extract of THYROID upon polyneuritic pigeons, and the metamorphosis of tadpoles. Seaman (Emily C.), Am. J. Physiol. (Balt.), 1920, **53**, 101-108.

A study to ascertain if the thyroid contained water-soluble vitamines. Fresh glands were extracted with 95 per cent alcohol and made 0.8 per cent acid with HCl. After various manipulations a water extract is obtained, one cubic centimeter of which contains 0.05 mg. of iodine and 0.435 per cent of nitrogen. The whole extract gave marked and rapid curative results when fed to polyneurotic pigeons. Improvement began within six hours. When the vitamine fraction was removed by the phosphotungstic acid method, the extract no longer had a curative effect. A "residue" containing the same amount of iodine was without effect, showing it was not the iodine which produced the results. The effect of the

whole extract on the metamorphosis of tadpoles is very marked. "The limb buds appeared within eight hours, and complete metamorphosis with the bulging eyes and disappearance of the tail within four days." Control experiments with the thyroid "residue" were negative.—T. C. B.

(THYROID) Syndrome de Basedow et tuberculose. Sergent (E.), Paris méd., 1920, **2**, 80-84.

The tendency of Graves' disease to simulate tuberculosis, especially in the female sex at puberty and the menopause, is emphasized by Sergent, who points out that in such cases the clinical picture of Graves' disease may be complete or only minor signs may be present. In both pulmonary tuberculosis and hyperthyroidism the following symptoms may be found either separately or in combination, viz.: an unsettled temperature, an unstable pulse usually characterized by attacks of more or less marked tachycardia, variations of the blood pressure, irregular menstruation, flushed face, sweating, loss of flesh, fatigue, attacks of abdominal pain and diarrhoea, cough, and shortness of breath. Sergent concludes that at both extremes of the sexual life of women the possibility of hyperthyroidism should be borne in mind, and that the presence of pulmonary tuberculosis should be admitted only if there are definite proofs of its existence. —Med. Sc. Abst. & Rev., **3**, 213.

Experimental treatment of dementia precox with THYROID preparation (Mededeelingen over proeven van behandeling der dementia praecox met schildklierpreparaten). Schnitzler (J. G.), Nederl. Tijdschr. v. Geneesk. (Amsterdam), 1916, **60** (I), 1179-1181.

In 1914 Lemei, a Dutch psychiatrist, reported splendid results with organotherapy (thyroid) in dementia precox. Schnitzler tried this in 22 typical cases but with no definite success.—J. K.

(THYROID) Results of operations for Graves' disease with reference to the incidental blood conditions and vascular system. Sekiguchi (Shigeki) & Ohara (Hachiro), Tohoku J. Exp. Med. (Sendai), 1920, **1**, 192-210.

This report is based upon a study of fifteen cases of which ten were operated on. The authors were unable to find any pronounced alterations in red blood cells or leucocytes before operation, though the time of coagulation of the blood is increased about two minutes as compared with the normal. After operation the neutrophile leucocytes increase for a short time and the lymphocytes decrease, but this condition is noted in other diseases. When cardiac dilation occurs it is most prominent on the left ide. The systolic and diastolic pressure varies within normal limits, but the pulse amplitude seems to be increased.—E. V. C.

(THYROID) Humoral symptoms of the Basedow's disease (I sintomi umorali del morbo di Basedow). Siciliano (L.), Riv. Crit. di Clin. Med. (Firenze), 1920, **21**, 307-311.

Siciliano reviews the several modifications of the blood (leukopenia and lymphocytosis and mononucleosis), the histological modifications of the **thyroid**, the variation in iodine content, the increase of **adrenin**, the glycosuria and hyperglycemia, the basal metabolism and Aberhalden's complement deviation, and finally the action of iodine on the thyroid function. All these researches are of help in the diagnosis of Basedow's disease, yet none of them is final, as a positive reaction can also be obtained in forms of pure hyperthyroidism (not yet pathological), so that to eliminate every doubt one has to go back to the study of the clinical symptoms and to the study of the course of the disease.—G. V.

(THYROID) Exophthalmic goiter in its hereditary and familial aspects (Goitre exopthalmique héréditaire et familial). Souques (A.) & Lermoyez (J.), Rev. neurol. (Paris), 1918, **34**, 320-321.

A presentation of four cases of hereditary and familial exophthalmic goiter. Three others of this family of 15 have Basedow's disease. The occurrence of this grouping is attributed to an hereditary predisposition rendering the thyroid more accessible to various and sundry toxic infections.—F. S. H.

(THYROID) Goitre. Starr (F. N. G.), Graham (R. R.) & Robinson (W. L.), Canad. M. Ass. J. (Toronto), 1920, **10**, 977-982d.

The following classification of goitre based on a clinical and pathological study of 300 cases, is advocated.

I. Diffuse
   (a) Colloid
   (b) Hyperplasia (exophthalmic)

II. Tumours
   (a) Adenoma
      1. Simple
      2. Colloid
      3. Hyperplastic
   (b) Malignant
      1. Carcinoma
      2. Sarcoma

Surgical treatment is advocated.—L. G. K.

(THYROID) Some remarks on subthyroidism. Stiell (W. F.), Practitioner (Lond.), 1920, **105**, 146-149.

Many minor ailments, such as constipation, neuralgia, mental apathy, menorrhagia, pseudo-asthma, chilliness and palpitations are frequently due to benign (mild) subthyroidism and are relieved

by administration of thyroid extract. Stiell attempts to explain the improvement by the relief of slight myxedematous infiltration of the cortical nerve cells, nerve fibers, meninges in the case of headache; of the frontal lobe in mental apathy; of the uterus in menorrhagia; of the bronchioles in pseudo-asthma, etc. For these same symptoms Arbuthnot-Lane have removed the colon, relieving the toxemia from colonic stasis—but thyroid frequently relieves the stasis and therefore the toxemia.—H. L.

(THYROID) Struma maligna. Streiszler, Wien. klin. Wchnschr., 1920, **33**, 763.

Demonstration of a case showing many metastases in the bones. The primary goiter did not exhibit signs of malignancy. Two years after the case was first observed the patient suffered a spontaneous fracture of the right femur, the cause of which was not detected. Two years later a soft tumor of the left knee and of the sternum developed. A piece of tissue was taken for examination and a diagnosis of struma malignum was made. The primary goiter was removed and a retrosternal lobe, showing marked symptoms of malignant degeneration, was found.—J. K.

THYROID insufficiency and hypersomnia (Hipersomnia e insuficiencia tiroidea). Udaondo (C. B.), Rev. de la. Asoc. méd. Argent. (Buenos Aires), 1920, **33**, 235-244.

A report of two cases of hypothyroidism, one a woman of 29 and the other a man of 33, giving a history of a tendency to fall asleep at all times, although they had from 10 to 12 hours' sleep each night. Thyroid therapy (0.06 grams daily, then increased) cured the complaint.—B. A. H.

(THYROID DIABETES) Goiter in Graves' disease (Basedow-struma). Urban, Wien. klin. Wchnschr., 1920, **33**, 718.

The patient was a woman of 45, with Graves' disease and diabetes. Half of the goiter was removed. After several days the diabetes had disappeared; even the administration of large doses of carbohydrate did not produce glycosuria. The symptoms of Graves' disease improved rapidly after the operation.—J. K.

(THYROID) A study of the distribution of iodine between cells and colloid in the thyroid gland. II. Results of study of dog and human thyroid glands. Van Dyke (Harry Benjamin), J. Biol. Chem. (Balt.), 1921, **45**, 325-332.

This paper is a report of the distribution of iodine in the thyroid glands of normal and iodine fed dogs as well as in human glands obtained from individuals subjected to operation for toxic goiter.

It was found that following the method of Tatum the concentration of intracellular iodine is independent of the suspending medium, whether that is pure Ringer's solution, Ringer's solution containing iodine—rich colloid material, or homologous blood serum, and that autolysis apparently did not occur to any extent during the period of extraction.

The ratio value of the distribution of iodine between cells and colloid was found to be relatively constant despite great variations in morphology and iodine content of the glands examined. The ratio value for the dog's thyroid gland seems quite constant and is much lower than that of beef or sheep, while that for man lies between the two groups.—F. S. H.

Influence of THYROID extract and of other organ extracts on the metamorphosis and reproduction of CYCLOPS VIRIDIS and CYCLOPS SERRULATUS (Influenza dell'estratto di tiroide e di altri estratti organici sulla metamorfosi e riproduzione di Cyclops viridis e Cyclops serrulatus). Vecchi (Anita), Arch. di Fisiol. (Firenze), 1920, **17**, 105-136, 14 tab.

The author shows as a result of a large number of experiments on the crustacean, Cyclops, that feeding with various (mammalian?) organ extracts leads (1) to a marked abbreviation in the duration of the larval period, and (2) to a shortening of the time interval between the successive depositions of eggs by the female. These effects are exercised in the greatest degree by the extract of thyroid, then by that of **thymus**, and to a less extent by those of the **suprarenal** and **spleen. Ovarian** extract produces no well defined effects upon development—and may be compared in its action with the effect produced by a non-glandular substance such as fibrin. The duration of larval life in Cyclops viridis is about 28 days (20 to 34). Specimens allowed to hatch and undergo development in a thyroid medium metamorphose after 7 to 14 days; in thymus, after 11 to 17 days; in suprarenal and in spleen after 12 to 19 days. The experiments in which thyroid alone was fed in water were supplemented by experiments in which additional nutriment was supplied in the form of hay infusion containing the protozoan, Glaucoma. But the accelerative effect of the thyroid was still very apparent, although the period of development was thereby shortened both in experiments and in controls. Cyclops viridis completes 5 depositions of ova in water in a 39-day period, in a thyroid medium in 28 days. Those grown in thymus require 29 days, the controls (in water) 34 days; those in suprarenal 29 days, controls 34 days; those in spleen 30 days, controls 35 days. Negative results as regards development were obtained by the use of ferric chloride in low concentrations (Cf. however, positive results of Urbinati on Cyclops macrunes, 1913; Bios, **1**, 191-275). The author concludes from the results of his experi-

ments with Cyclops that the effects observed are probably due to specific organ hormones which normally promote metabolism, since they appear to exercise their effects in diverse degrees—certain ones giving marked positive results, others being indifferent.

—F. S. H.

(THYROID) Paratuberculosis of the endocrine type (La paratuberculosis de tipo endocrino). Viton (J. J.), Rev. de la Asoc. med. argen. (Buenos Aires), 1920, **32**, 239-248.

Viton believes that patients which become better after the injection of tuberculin $1x10^{-20}$ are tuberculous and is of the opinion that many cases of hyperthyroidism are of tubercular origin.

—B. A. H.

(THYROID) The interpretation of basal metabolism with special reference to hypothyroidism and hyperthyroidism. Wade (B. N.), Northwest Med. (Seattle), 1920, **19**, 175-178.

Wade refers briefly to the work of Gephart, Dubois, Benedict and Carpenter in developing the clinical application of basal metabolism estimations. So far the value of such determinations seems to be confined to lesions of the thyroid gland.

"In the treatment of hypothyroidism the aim should be to find the minimal dose of thyroxin or thyroid extract necessary to maintain the normal or average metabolic rate, and this can be better regulated by basal metabolism determinations than by the symptoms or signs presented by the patient." "Lowered metabolism is usually present for a variable length of time before the symptoms of hypothyroidism appear, and also an increased metabolism may be present for a variable length of time before symptoms of hyperthyroidism appear. Therefore the basal metabolic rate is a far better index of the degree of severity of hypo- and hyperthyroidism than the symptoms would indicate. There is also no definite relation between the metabolic rate and the severity of the symptoms. Severe cases of thyrotoxicosis as evidenced by rates of 25 to 50 per cent above normal may show only mild signs and symptoms and vice versa. Some symptoms such as exophthalmus or tremor may persist even though the metabolic rate has been reduced to normal. Basal metabolism estimations are therefore of great value in diagnosis, prognosis and in determining when and how much to operate, and in controlling the results of operations, x-ray therapy or other purely medical measures. The author advises repeated determinations for the sake of accuracy because of the fluctuations that occur and the correlation as far as possible of these figures with the signs and symptoms exhibited by the patient.—H. L.

(THYROID) The leucocytic picture after injections of iron and thyroid preparations (Das relative weisse Blutbild nach Injectionen von Eisen und Schilddrüsenpräparaten). Waser (A.), Ztschr. f. Biol. (München), 1920, **71**, 107-116.

Subcutaneous injections of thyroid extract cause an increased formation of polymorphonuclear leucocytes. The number of lymphocytes decreases. Therefore the total number of colorless corpuscles remains the same. Phys. Abst., **5**, 365.

On the heredity of diseases conditioned by VAGOTONIA (Zur Frage der Erblickeit vagotonisch bedingter Krankheiten). Heissen (F.), Münch. med. Wchnschr., 1920, **67**, 1406-1407.

Vagotonia is often hereditary or familial. Endocrine causes, exudative diathesis, and other conditional causes are of importance.—J. K.

(VAGOTONIA) The use of atropine in the treatment of the hypertonic infant. Kaiser (A. D.), N. York M. Jour., 1920, **112**, 971-973.

The hypertonic condition (vagotonia) in children is manifest by irregular vomiting, at times by visible peristalsis, muscular irritability, constipation, malnutrition, insomnia and crying. These manifestations of hypertonicity are not the result of diet and may be controlled by the administration of atropine.—H. W.

Clinical aspects of VAGOTONIA and SYMPATHICOTONIA (Influencia de la Vagotonia y de la Sympateticotonia en la Clinic). Quimper (A. H.), Cron. méd. (Lima), 1920, **37**, 300-304.

The clear and concise exposition of the relations between sympathicotonia and vagotonia indicates the importance of its study, especially for visceral neuralgia and for the interpretation of the syndromes according to which the individual may have a constitution subject to vagotonia or sympathicotonia.—I. O.